Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

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Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

EDITOR, R. H. KAMPMEIER, M.D.
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VOLUME 50

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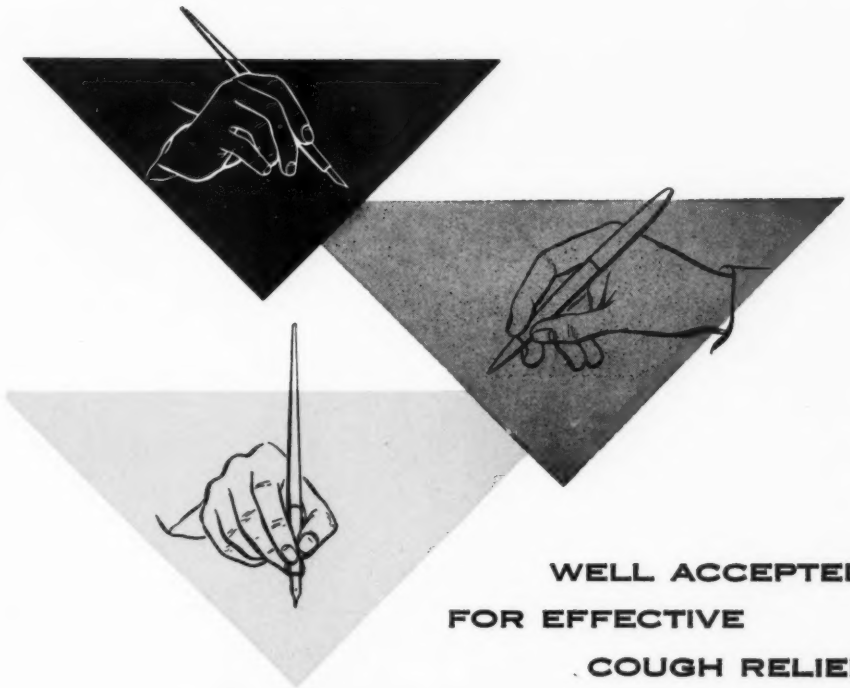

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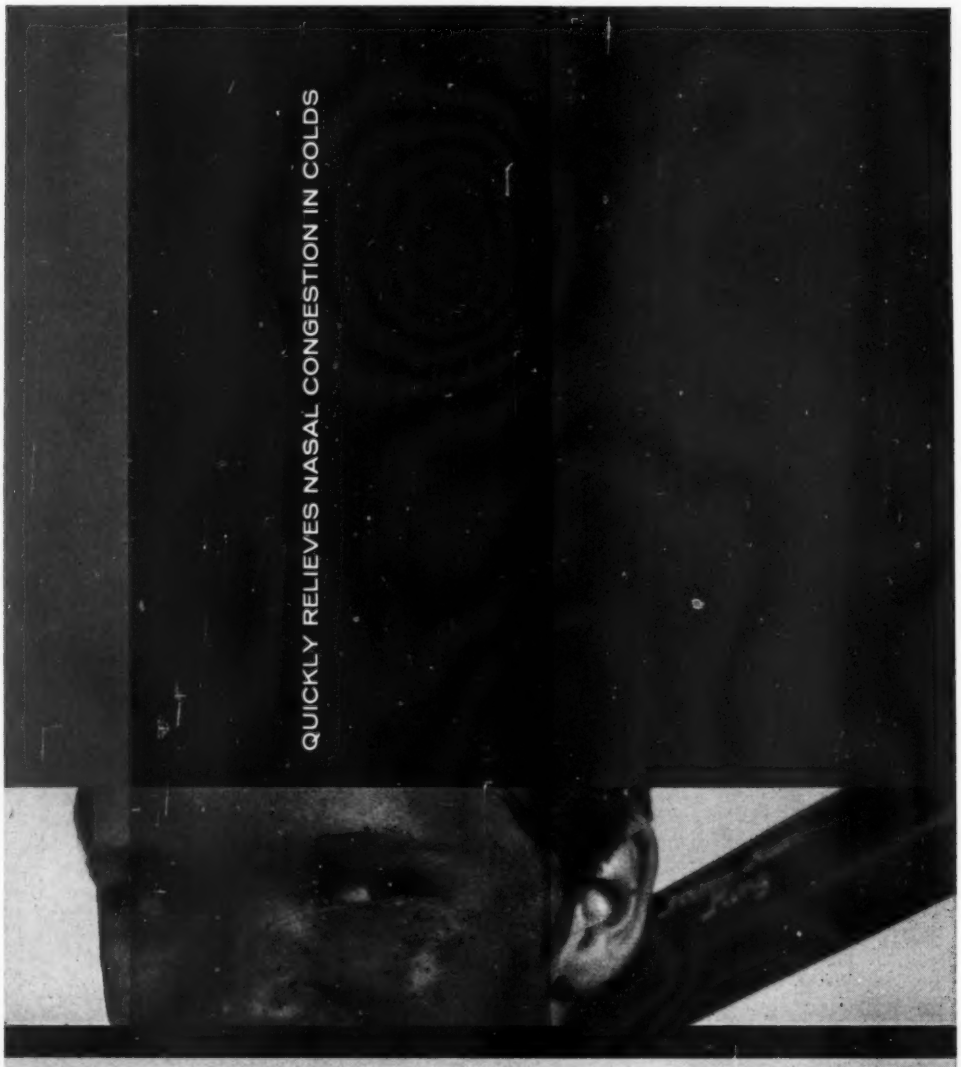

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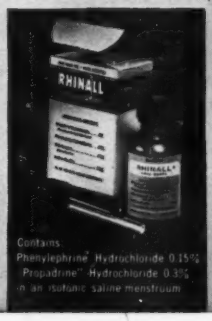

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*Stewart, B. L., and Rowe, H. J.: J. Am. M. Ass. **160**:1221, 1956.

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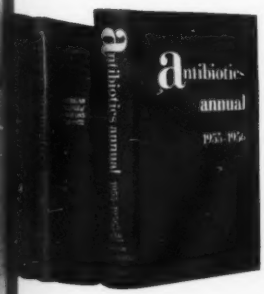

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1. Romansky, M.J., et al., Antibiotics Annual 1955-1956, p. 48,
2. Waddington, W. S., Maple, F. C., and Kirby, W. M. M., A.M.A. Archives of Internal Medicine, 1954, p. 556.

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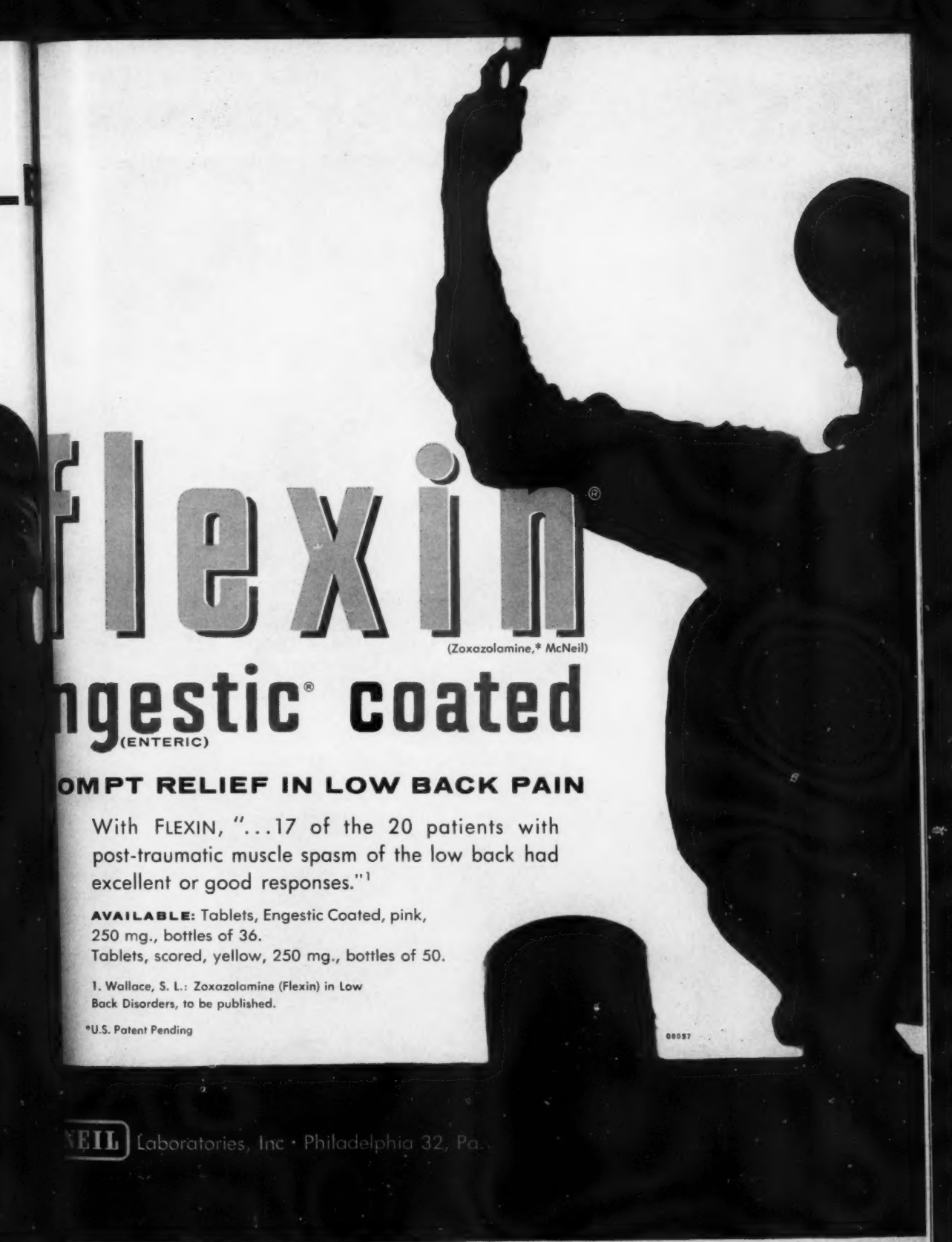

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1. Wallace, S. L.: Zoxazolamine (Flexin) in Low Back Disorders, to be published.

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*Ferguson, J. T.: J. Am. Geriatrics Soc. *4*:1080, 1956.

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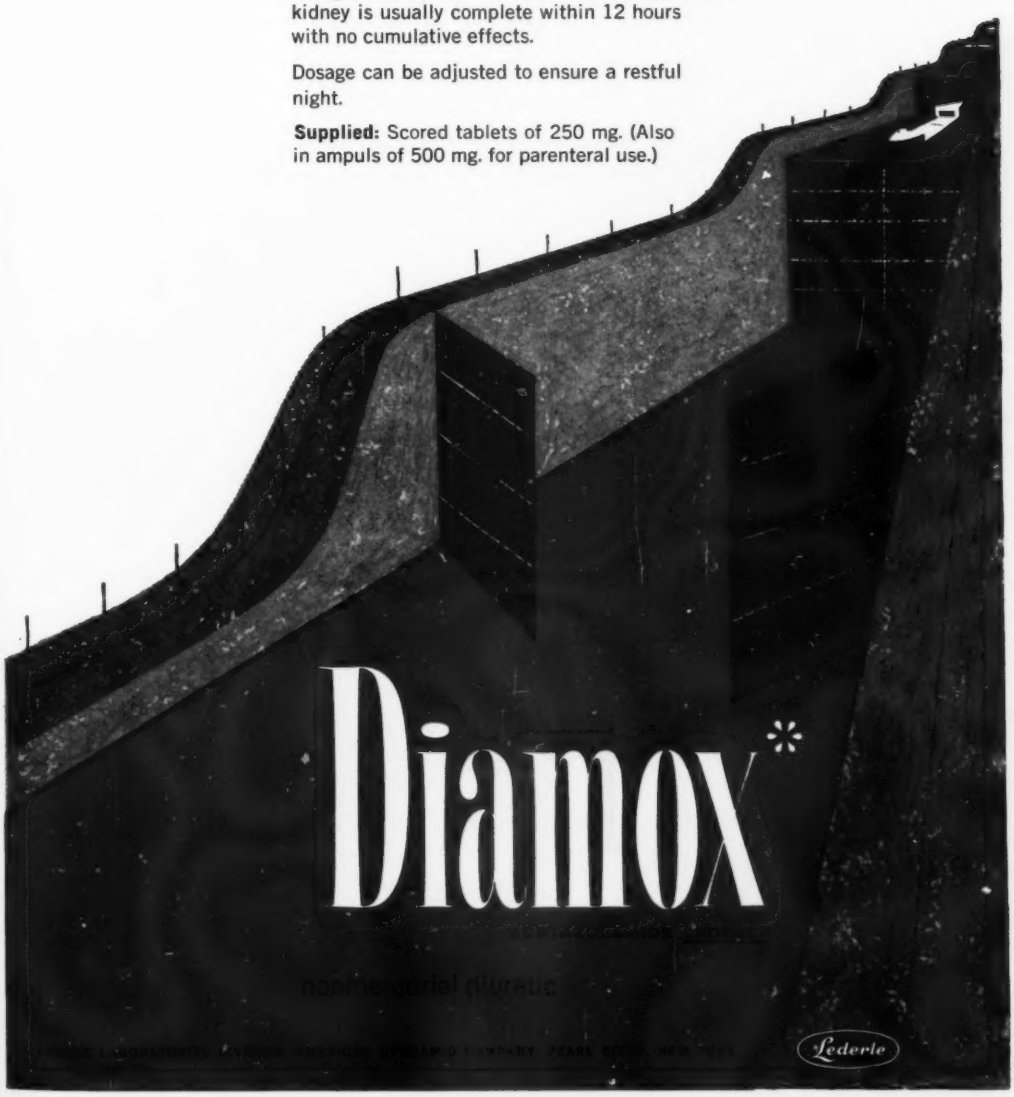

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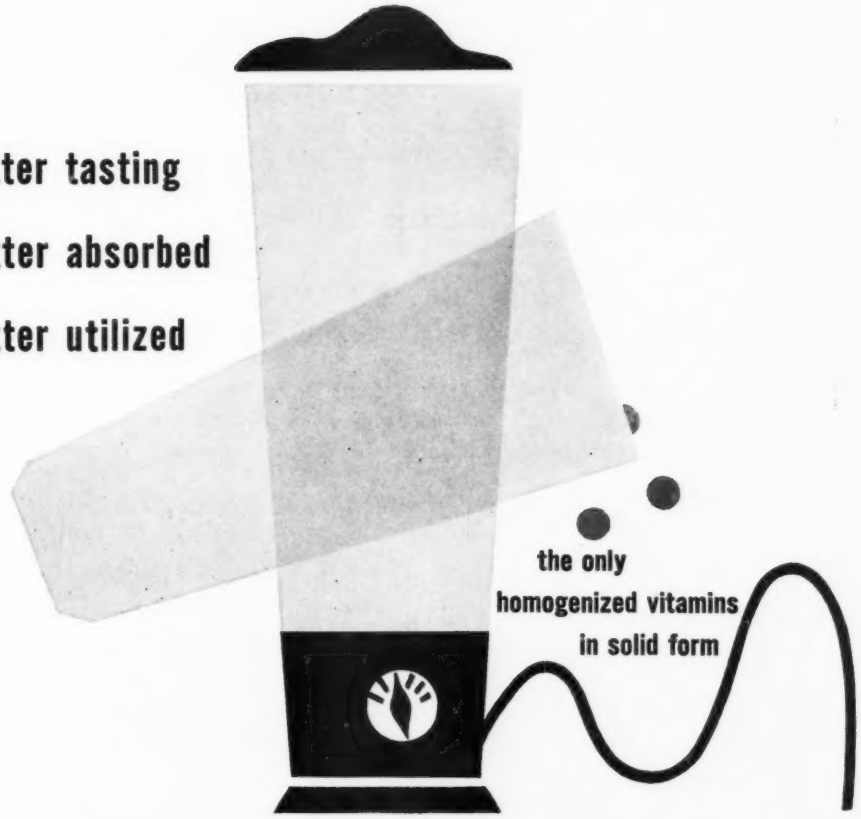

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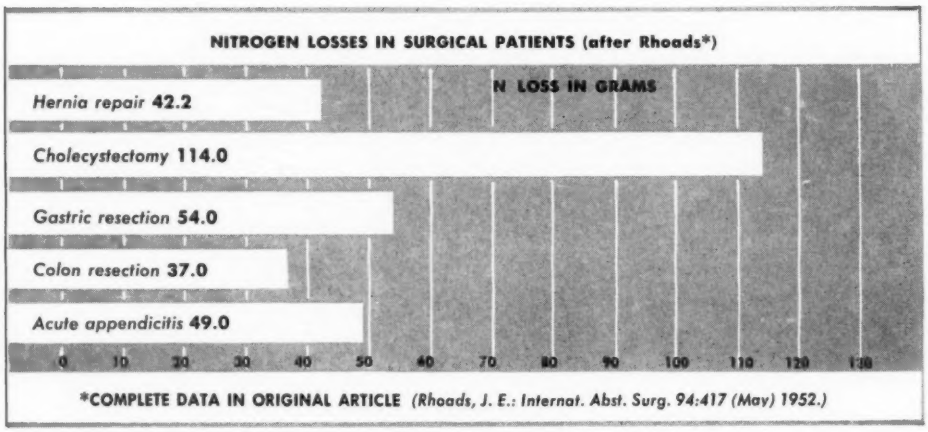
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Cholecystectomy 114.0
Gastric resection 54.0
Colon resection 37.0
Acute appendicitis 49.0
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*COMPLETE DATA IN ORIGINAL ARTICLE (Rhoads, J. E.: Internat. Abst. Surg. 94:417 (May) 1952.)

Patients about to undergo extensive surgery[1] frequently have negative nitrogen balance and protein deficiency. And after any severe trauma, including extensive surgery, the rate of protein breakdown is increased.

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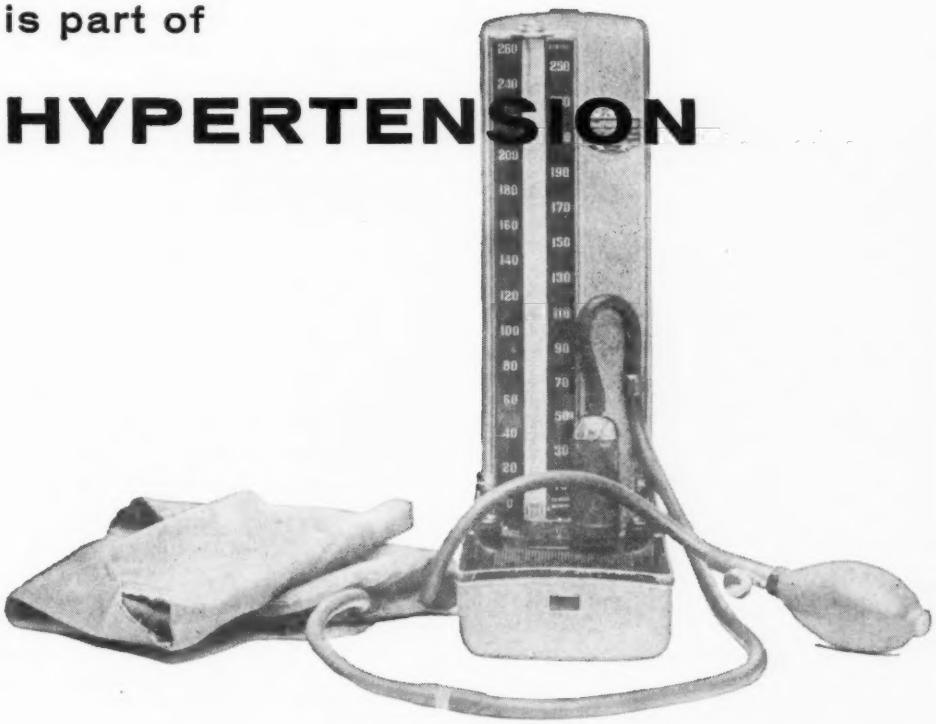

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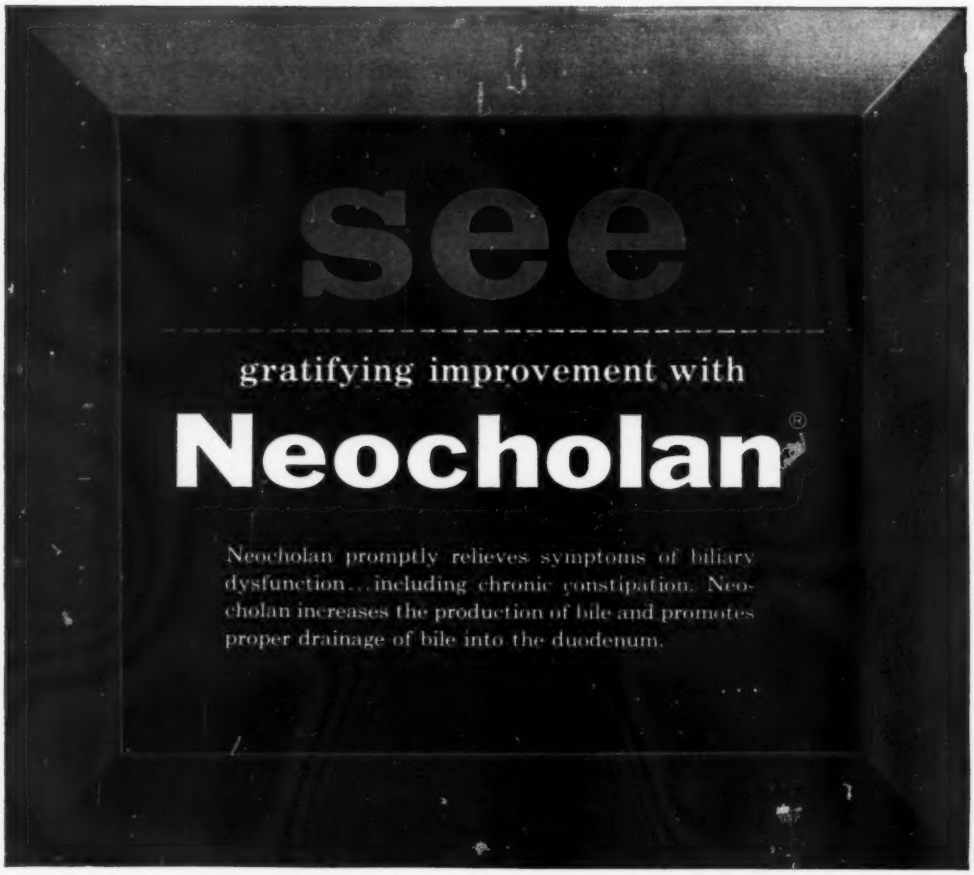
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Neocholan®
Neocholan promptly relieves symptoms of biliary dysfunction...including chronic constipation. Neocholan increases the production of bile and promotes proper drainage of bile into the duodenum.

1 or 2 Neocholan tablets t.i.d.—with meals—is the usual effective dosage. As symptoms improve the dose may be decreased to 1 or 2 tablets daily. Each Neocholan tablet supplies Dehydrocholic Acid 250 mg. (3¾ grs.); Homatropine Methylbromide 1.2 mg. (1/50 gr.); Phenobarbital 8.0 mg. (⅛ gr.). Bottles of 100 and 1000 coated, yellow tablets.

PITMAN-MOORE COMPANY *Division of Allied Laboratories, Inc.* **Indianapolis 6, Indiana**

". . . best results were obtained with women 35 to 55 years of age, who complained of anxiety, insomnia, chronic fatigue and despondency."[1]

Many physicians have reported favorable results with 'Compazine' in the mild or moderate mental and emotional conditions often associated with the menopause.

For example, in a series of 84 patients, Knoch and Kirk report outstanding results in women 35 to 55. The authors state that after 'Compazine' treatment, these women "were no longer fatigued, were sleeping well, had increased energy and showed a lively interest in their surroundings."

'Compazine' is S.K.F.'s new tranquilizer and antiemetic for everyday practice.

'Compazine' has shown minimal side effects.

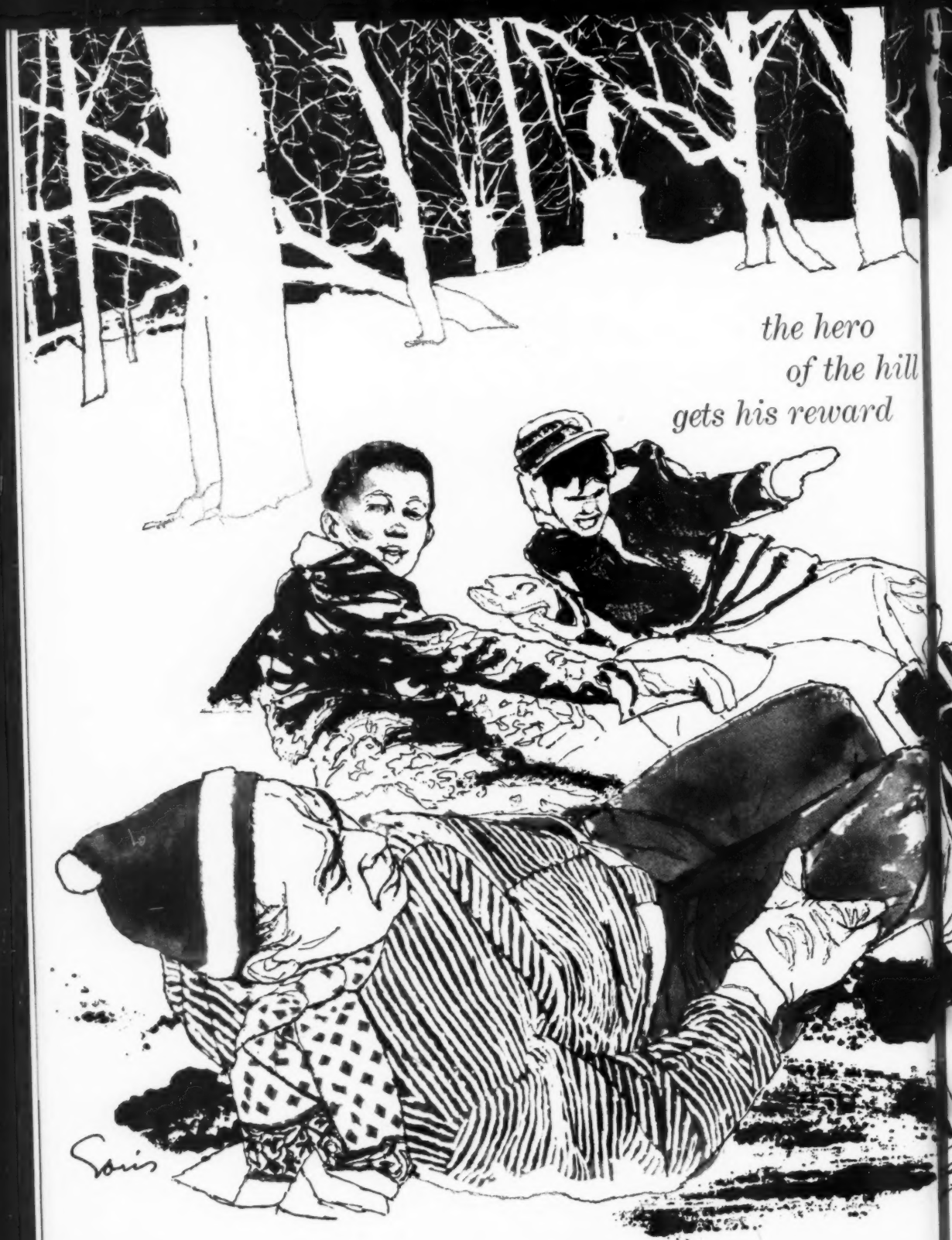
Compazine*

a true tranquilizing agent

Smith, Kline & French Laboratories, Philadelphia

1. Knoch, H.R., and Kirk, R.: Proclorperazine—A New Agent for the Treatment of Psychic Stress, in manuscript.

*Trademark for proclorperazine, S.K.F.



WT.M. 50-J-117

charleyhorse!

The pain Dad feels now is the beginning of tenosynovitis. With adequate early treatment he'll be able to stay on his job. Delaying therapy might result in the development of effusion and, later, calcification of ligaments or even periarthritis with severe pain and serious restriction of movement.

Immediate antirheumatic therapy is to be encouraged in the treatment of tenosynovitis, as it should be in the majority of other common rheumatic disorders, to alleviate pain and prevent progression of the disturbance to a point of irreversible damage.

SIGMAGEN provides doubly protective corticoid-salicylate therapy—a combination of METICORTEN® (prednisone) and acetylsalicylic acid giving additive antirheumatic benefit as well as rapid analgesic effect. These benefits are supported by aluminum hydroxide to counteract excess gastric acidity and by ascorbic acid, the vitamin closely linked to adrenocortical function, to help meet the increased need for this vitamin during stress situations.

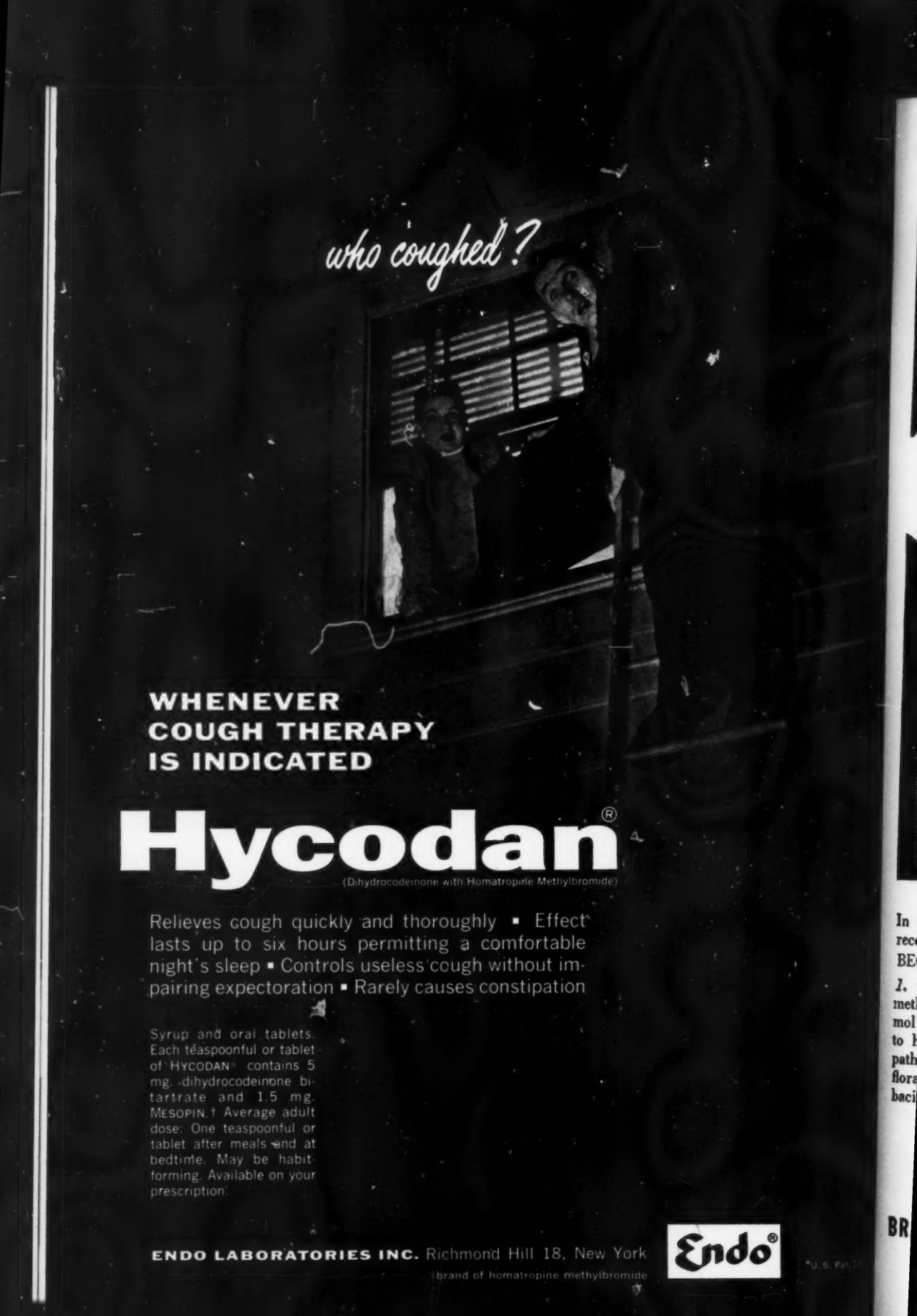
protective corticoid-salicylate therapy

SIGMAGEN*

corticoid-analgesic compound **Tablets**

for patients who go beyond their physical capacity

Schering



WHENEVER COUGH THERAPY IS INDICATED

Hycodan®

(Dihydrocodeinone with Homatropine Methylbromide)

Relieves cough quickly and thoroughly ▪ Effect lasts up to six hours permitting a comfortable night's sleep ▪ Controls useless cough without impairing expectoration ▪ Rarely causes constipation

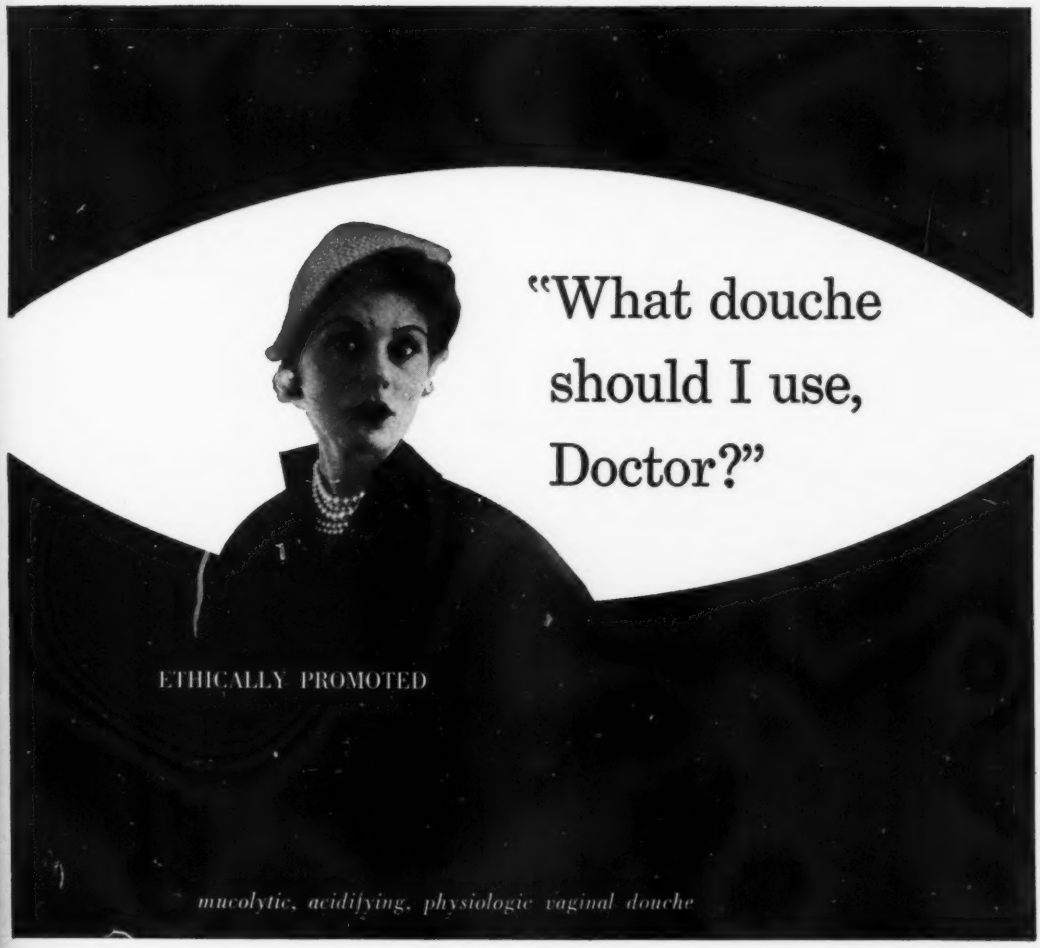
Syrup and oral tablets. Each teaspoonful or tablet of HYCODAN® contains 5 mg. dihydrocodeinone bitartrate and 1.5 mg. MESOPIN.† Average adult dose: One teaspoonful or tablet after meals and at bedtime. May be habit-forming. Available on your prescription.

ENDO LABORATORIES INC. Richmond Hill 18, New York

†brand of homatropine methylbromide

Endo®

*U.S. Pat.



In answer to questions about douching you can recommend META CINE with complete confidence BECAUSE META CINE:

1. is a safe, soothing douche (pH 3.5) containing methyl salicylate, eucalyptol, menthol, chlorothymol and PAPAIN to liquefy mucus. CITRIC ACID to help restore the proper acid pH, discourage pathogenic organism, promote normal vaginal flora. LACTOSE to feed the physiologic Doderlein bacilli.

2. is pleasant and refreshing to the patient . . . and deodorizing.

3. has a surface tension of 56 dynes/cm as compared to 72 dynes/cm for the usual vinegar douche.

4. is economical . . . only two teaspoonfuls to two quarts of water . . . supplied in eight-ounce containers.

5. is useful as a routine, cleansing douche, as an adjuvant when treating leukorrheal infections, and following cervical cauterizations and conizations.

UPON YOUR REQUEST *a free supply of instruction sheets will be sent for your convenience in advising patients on the correct douching technique.*

BRAYTEN PHARMACEUTICAL COMPANY, 3810 St. Elmo Avenue, Chattanooga 9, Tennessee

gentle is the word for Noludar

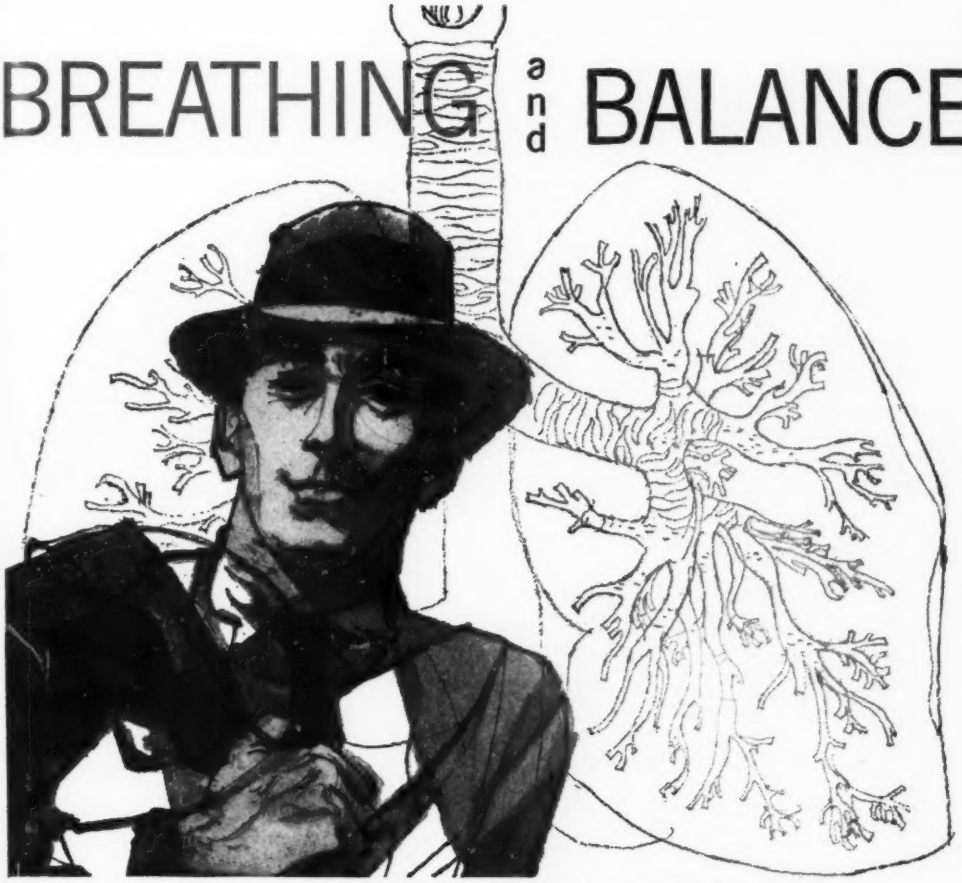
Mild, yet positive in action, Noludar 'Roche' is especially suited for the tense patient who needs to relax and remain clear-headed—or for the insomniac who wants a refreshing night's sleep without hangover. Not a barbiturate, not habit-forming. Tablets, 50 and 200 mg; elixir, 50 mg per teasp.

Noludar® brand of methyprylon (3,3-diethyl-5-methyl-2,4-piperidinedione)

ROCHE

Original Research in Medicine and Chemistry

BREATHING and BALANCE



in bronchial asthma

Sterane®

brand of prednisolone

whenever corticosteroids are indicated

provides restoration of breathing capacity — Relief of symptoms [bronchospasm, cough, wheezing, dyspnea] is maintained for long periods with relatively small doses.*

minimal effect on electrolyte balance — "in therapeutically effective doses . . . there is usually no sodium or fluid retention or potassium loss."* Lack of edema and undesirable weight gain permits more effective therapy particularly for those with cardiac complications.

Supplied: White, 5 mg. oral tablets, bottles of 20 and 100. Pink, 1 mg. oral tablets, bottles of 100. Both are deep-scored.

*Schwartz, E.: New York J. Med. 56:570, 1956.

PFIZER LABORATORIES, Brooklyn 6, New York
Division, Chas. Pfizer & Co., Inc.

AGE . . . In older people, chronic constipation and biliary dyspepsia are often the result of decreased food and water intake, physical inactivity, intestinal muscle atonicity, increased anorectal disorders, biliary stasis.

for biliary dyspepsia and constipation

OCCUPATION . . . Among sedentary workers, chronic constipation and impaired digestion are often the result of lack of exercise and improper eating habits which retard normal peristaltic action in the gastrointestinal tract.

Tablets of Caroid and Bile Salts with Phenolphthalein are specifically formulated to provide a 3-way, comprehensive approach to the problem of impaired digestion and elimination.

1. CHOLERETIC **2. DIGESTANT** **3. LAXATIVE**	Bile salts stimulate biliary flow for improved fat emulsification while Caroid steps up protein digestion up to 15%. Gentle stimulant laxatives induce formed, easily passed stools.

For patients who cannot or will not be managed by diet and exercise, Caroid and Bile Salts helps establish normal physiological patterns.

samples available on request

AMERICAN FERMENT COMPANY, INC., 1450 BROADWAY, NEW YORK 18, N. Y.

CAROID® AND BILE SALTS *Tablets*

severe asthma

is usually aggravated

and prolonged

by a strong emotional overlay

In one study, 'Thorazine' relaxed and improved 11 of 12 patients within one hour after injection . . . in one case "appeared to be life-saving."[1]

'Thorazine' promptly alleviates the emotional stress which may precipitate, aggravate or prolong an asthmatic attack. It enables the patient to sleep, yet does not depress respiration.

Available: Ampuls, Tablets, Syrup (as the hydrochloride), and Suppositories (as the base).

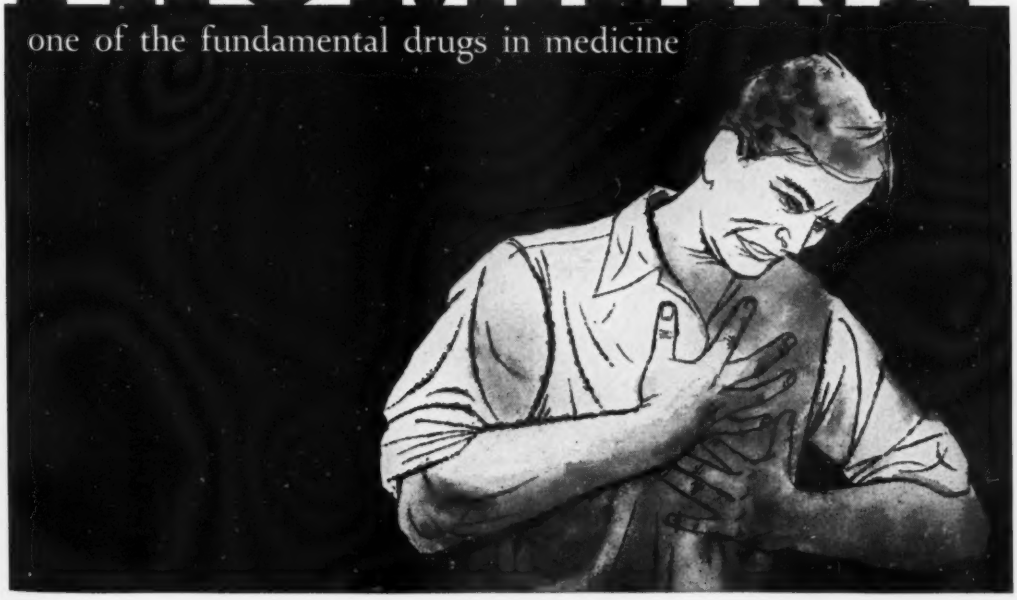
Smith, Kline & French Laboratories, Philadelphia

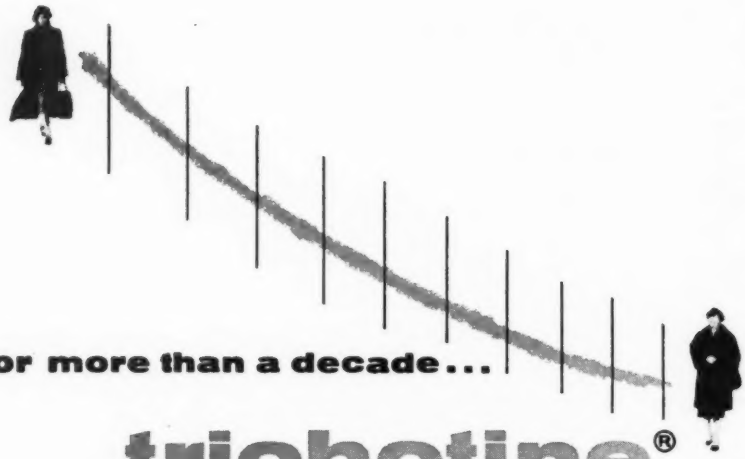
1. Ende, M.: Am. Pract. & Dig. Treat. 6:710 (May) 1955.

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

THORAZINE*

one of the fundamental drugs in medicine





for more than a decade...

trichotine®

...proved effective in vulvovaginal therapy

Trichotine—more than a decade ago—pioneered in newer, more effective vulvovaginal therapy by combining the multiple advantages of sodium lauryl sulphate with the recognized values of such specific or adjunctive agents as sodium perborate, sodium borate, thymol, eucalyptol, menthol and methyl salicylate.

Extensive clinical experience has proved its efficacy in trichomonas vaginalis vaginitis, subacute and chronic cervicitis, vulvovaginal moniliasis, non-specific leukorrhea, and pruritus vulvae.

Trichotine douches may be prescribed as often as indicated—excellent also for postmenstrual or postcoital hygiene. Concentrated solutions are useful for clean-up or swab treatments in office. Hot packs are often quickly effective in pruritus vulvae.

A DETERGENT · A BACTERICIDE AND FUNGICIDE · AN ANTIPRURITIC

AN AID TO EPITHELIZATION · AN AESTHETIC AND PSYCHOSOMATIC ADJUNCT

Sample and literature on request *Available in jars of 5, 12 and 20 oz.*

the fesler co., inc., 375 Fairfield Ave., Stamford, Conn.

XYLOCAINE
HYDROCHLORIDE 1%
XYLOCAINE
HYDROCHLORIDE 0.5%
with EPINEPHRINE 1:100,000
to try it .....
XYLOCAINE
HYDROCHLORIDE 2%
XYLOCAINE
HYDROCHLORIDE 1%
with EPINEPHRINE 1:50,000
STERILE AQUEOUS SOLUTION FOR INJECTION
with EPINEPHRINE 1:100,000

fastest acting local anesthetic— as safe as it is effective

How safe is Xylocaine? In five years, over 500,000,000 injections of Xylocaine HCl Solution have been given for local anesthesia. "The apparent clinical safety of Xylocaine is gratifying, for without this quality, its additional properties would not warrant an enthusiastic report. Nor would safety alone call for a high recommendation unless additional desirable properties were to be found. The truth of the matter is, however, that Xylocaine approaches the ideal drug more closely than any other local anesthetic agent we have today."*

How effective is Xylocaine? Xylocaine HCl Solution produces more rapid, complete, and deeper anesthesia than other local anesthetics used in equivalent doses. By infiltration, Xylocaine gives a wide area of analgesia, and surrounding tissues are also anesthetized. The long duration of Xylocaine action reduces the need for additional injections. At the same time, it assures greater comfort to your patients for a longer period – often when they need it most.

How does Xylocaine fit into my practice? Xylocaine is the ideal agent for *local infiltration anesthesia* because it is safe, fast acting and of long duration. It is used routinely in daily practice for countless minor surgical procedures such as closure of lacerations, removal of cysts, moles and warts; treatment of abscesses; and in the reduction of fractures.

....is to use

XYLOCAINE®

It has also become the choice of many physicians for *therapeutic interruption of nerve function by temporary nerve blocks* in herpes zoster, subdeltoid bursitis, fibrositis, myalgia of shoulder muscles, periarthritis due to trauma, and painful postoperative scars. The relief of pain in these conditions at times appears to be the most important part of treatment.

The remarkable *topical anesthetic* properties of Xylocaine HCl Solution further enhance its usefulness for minor operations. Topical anesthesia can be obtained by spraying, by applying packs, by swabbing, or by instilling the solution into a cavity or on a surface.

Xylocaine HCl Solutions are available in 2 cc. ampuls, 20 cc. and 50 cc. vials in strengths of 0.5%, 1% and 2%, with or without epinephrine.

Bibliography of approximately 300 Xylocaine references upon request.

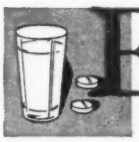
*Southworth, J. L., and Dabbs, C. H.: Xylocaine: a superior agent for conduction anesthesia, Anesth. & Analg. *32*:159 (May-June) 1953.

Astra Pharmaceutical Products, Inc., Worcester 6, Mass.

In Angina Pectoris

The Attacks Lessen and The Patient Loses His Fear

Pentoxylon®



Each long-acting tablet provides the sustained coronary vasodilating effect of 10 mg. pentaerythritol tetranitrate (PETN) as well as the tranquilizing, anxiety-relieving and pulse-normalizing action of 1 mg. Rauwiloid® (alseroxylon).

- Reduces incidence of attacks
- Reduces severity of attacks
- Reduces or abolishes need for fast-acting vasodilating drugs
- Reduces tachycardia
- Reduces blood pressure in hypertensives, not in normotensives
- Increases exercise tolerance
- Produces demonstrable ECG improvement
- Exceptionally well tolerated
- Minimal side actions
- Dosage: one to two tablets q.i.d., a.c. and h.s.

And

for faster relief of the acute attack

Medihaler-Nitro™

octyl nitrite (1%) in aerosol solution

For faster, safer, and more lasting relief of acute anginal attacks . . . Measured-dose inhalation provides instantaneous coronary vasodilatation via the lungs . . . one inhalation equivalent to 1/100 gr. nitroglycerin . . . fewer side actions than amyl nitrite . . . pocket-sized aerosol set . . . each 10 cc. bottle delivers 200 metered doses.

Riker

LOS ANGELES

for normal, healthy, comfortable pregnancies

Walker
100 CAPSULES
PRECALCIN
LACTATE
A DIETARY SUPPLEMENT
FOR USE DURING PREGNANCY AND LACTATION
EACH CAPSULE CONTAINS:
CALCIUM LACTATE Anhydrous 450.00 mg
VITAMIN A Crystalline 2,000 U.S.P. Units
VITAMIN D3 Crystalline 400 U.S.P. Units
THIAMINE HCl 3.00 mg
RIBOFLAVIN 2.00 mg
NIACINAMIDE 10.00 mg
ASCORBIC ACID 30.00 mg
CALCIUM PANTOTHENATE 2.50 mg
PYRIDOXINE HCl 1.00 mg
FOLIC ACID .33 mg
VITAMIN B12 conc. activity equiv. to 1.00 mcg
FERROUS GLUCONATE 100.00 mg
TRACE ELEMENTS*
*As Added Micronutrients
MICRONUTRIENTS
Copper as Copper Sulfate 2 mg.; Manganese as Manganese Sulfate 2 mg.; Cobalt as Cobalt Sulfate .04 mg.; Zinc as Zinc Oxide 2 mg.; Magnesium as Magnesium Sulfate 2 mg.; Molybdenum as Sodium Molybdate .04 mg.; Iodine as Potassium Iodide .02 mg.; and Fluorine as Calcium Fluoride .04 mg.
DOSE: 1 capsule three times daily, or as prescribed.
(SEE REAR PANEL)
WALKER LABORATORIES, INC.
MOUNT VERNON, NEW YORK, U.S.A.
Walker
100 CAPSULES
PRECALCIN
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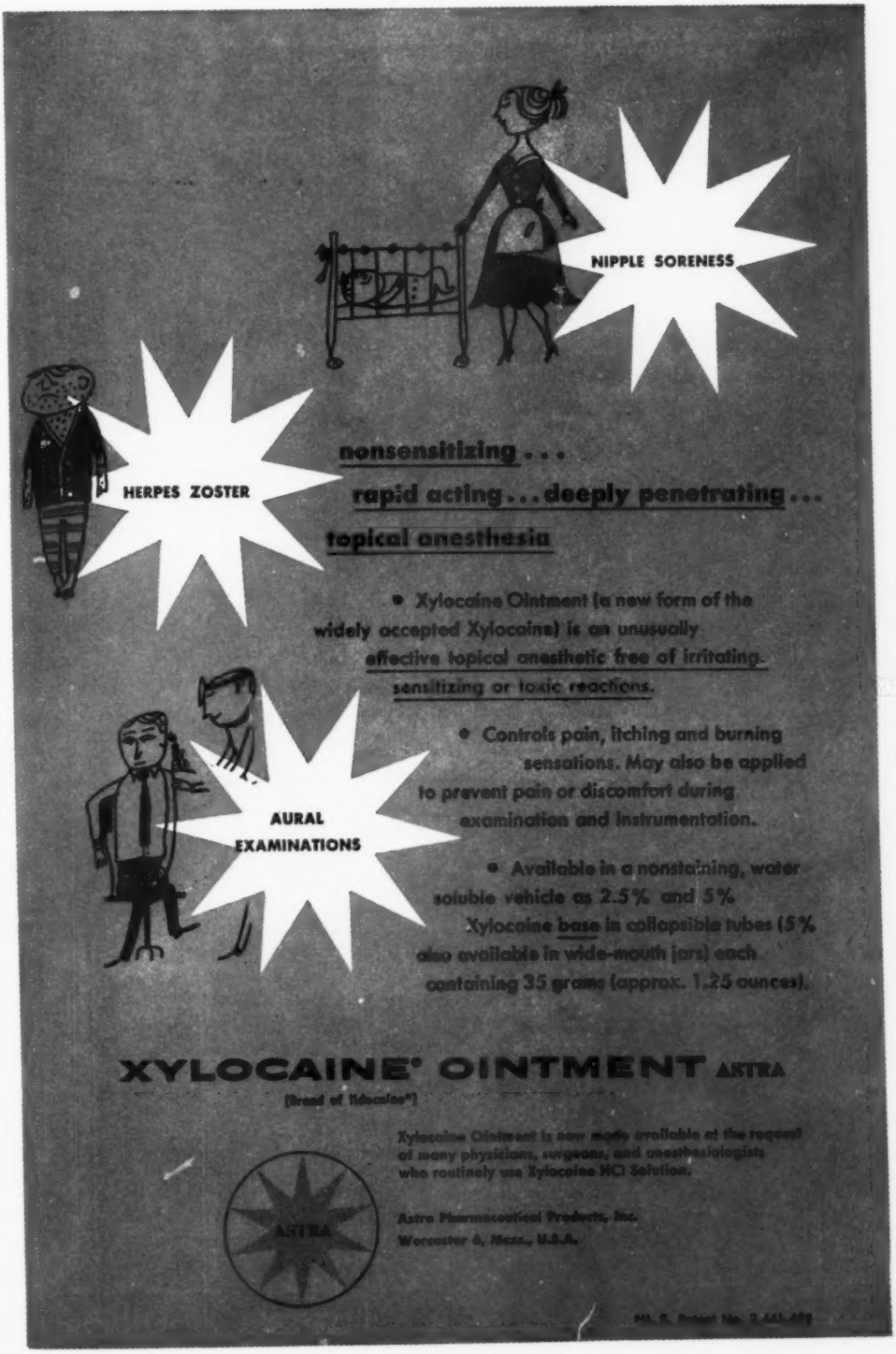
LABORATORIES, INC. · MOUNT VERNON, N.Y.

PHOSPHORUS-FREE, HIGH-POTENCY DRY-FILL CAPSULES WITH "BUILT-IN" ANTIANEMIA FACTORS

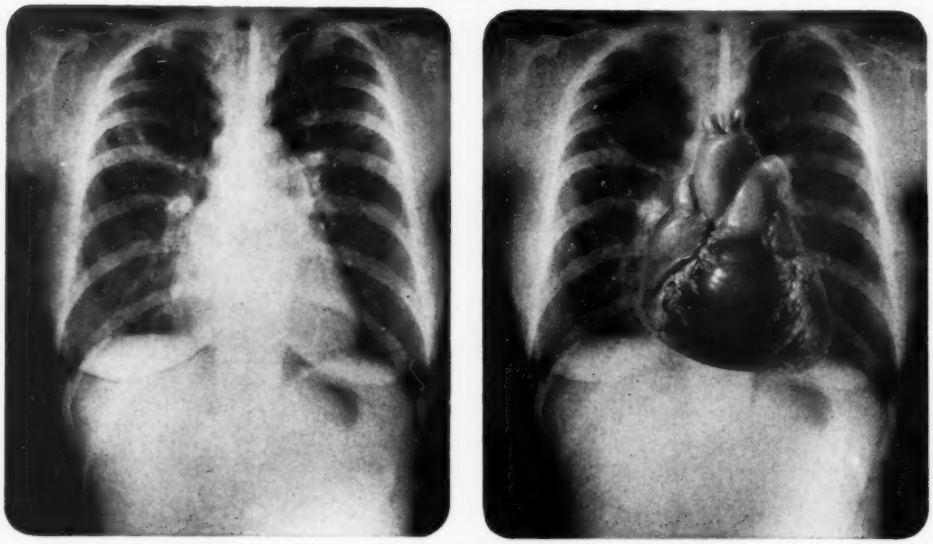
now with FLAVINOL
33.3 mg. per capsule

Walker LABORATORIES, INC., MOUNT VERNON, N. Y., U. S. A.


NIPPLE SORENESS
HERPES ZOSTER
nonsensitizing . . .
rapid acting . . . deeply penetrating . . .
topical anesthesia
• Xylocaine Ointment (a new form of the widely accepted Xylocaine) is an unusually effective topical anesthetic free of irritating, sensitizing or toxic reactions.
• Controls pain, itching and burning sensations. May also be applied to prevent pain or discomfort during examination and instrumentation.
• Available in a nonstaining, water soluble vehicle as 2.5% and 5% Xylocaine base in collapsible tubes (5% also available in wide-mouth jars) each containing 35 grams (approx. 1.25 ounces).
AURAL EXAMINATIONS
XYLOCAINE® OINTMENT ASTRA
[Brand of lidocaine*]
Xylocaine Ointment is now more available at the request of many physicians, surgeons, and anesthesiologists who routinely use Xylocaine HCl Solution.
ASTRA
Astra Pharmaceutical Products, Inc.
Worcester 6, Mass., U.S.A.

"A GOOD PRESENT DAY ALL-PURPOSE DIGITALIS...GITALIGIN ...A PREPARATION WHICH HAS A WIDER MARGIN OF SAFETY..."*

VISUAL HEART CLINIC—NUMBER ONE OF A SERIES



RHEUMATIC HEART DISEASE • MITRAL STENOSIS AND INSUFFICIENCY

ROENTGEN CONFIGURATION—Postero-anterior examination—moderate heart enlargement—right ventricular enlargement—prominence of pulmonary artery segment.

Taken from White Laboratories' Technical Exhibit, American Medical Association 105th Annual Meeting, Chicago, June 11-15, 1956.

Every year since 1950 when Batterman, et al., published the results of their study of 230 cardiac patients, clinical evidence has repeatedly confirmed the therapeutic advantages of GITALIGIN.

For initial digitalization and maintenance, GITALIGIN has proved to be "the digitalis of choice" for these significant reasons:

(1) Widest safety margin of any currently available digitalis glycoside (average therapeutic dose only 1/3 the toxic dose; in contrast, therapeutic doses of other preparations are approximately 2/3 toxic dose)
(2) Uniform clinical potency
(3) Moderate rate of dissipation
(4) Short latent period

Patients now being maintained with other cardiotonics can be easily switched to GITALIGIN: 0.5 mg. of GITALIGIN is approximately equivalent to 0.1 Gm. digitalis leaf, 0.1 mg. digitoxin, 0.5 mg. digoxin.

White's | GITALIGIN®

(WHITE'S BRAND OF AMORPHOUS GITALIN)

TABLETS—BOTTLES OF 30, 100, AND 1000 DROPS—30 CC. BOTTLES WITH DROPPER CALIBRATED FOR 0.05, 0.1, 0.2, 0.3, 0.4 AND 0.5 MG.

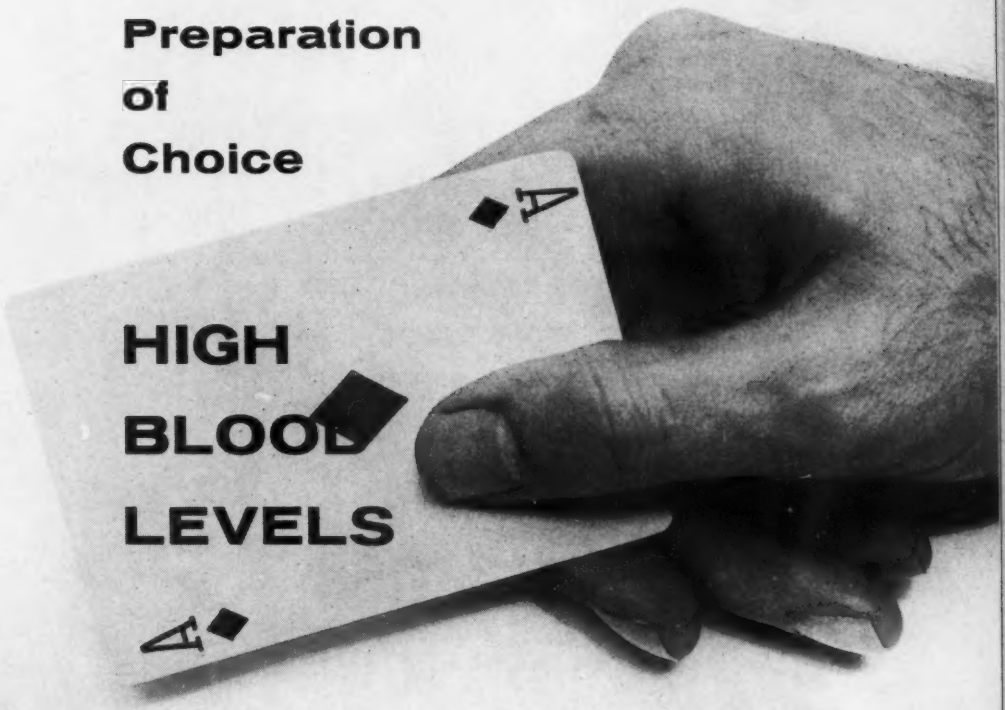
INJECTION—5 CC. AMPULS CONTAINING 2.5 MG. (0.5 MG. PER CC.) OF GITALIGIN, PACKAGES OF 3 AND 12 AMPULS.

*EHRLICH, J.C.: ARIZONA MED. 12:239 (JUNE) 1955. BIBLIOGRAPHY FURNISHED ON REQUEST

White Laboratories, Inc. Kenilworth, New Jersey

In Urinary-Tract Infections

Preparation of Choice

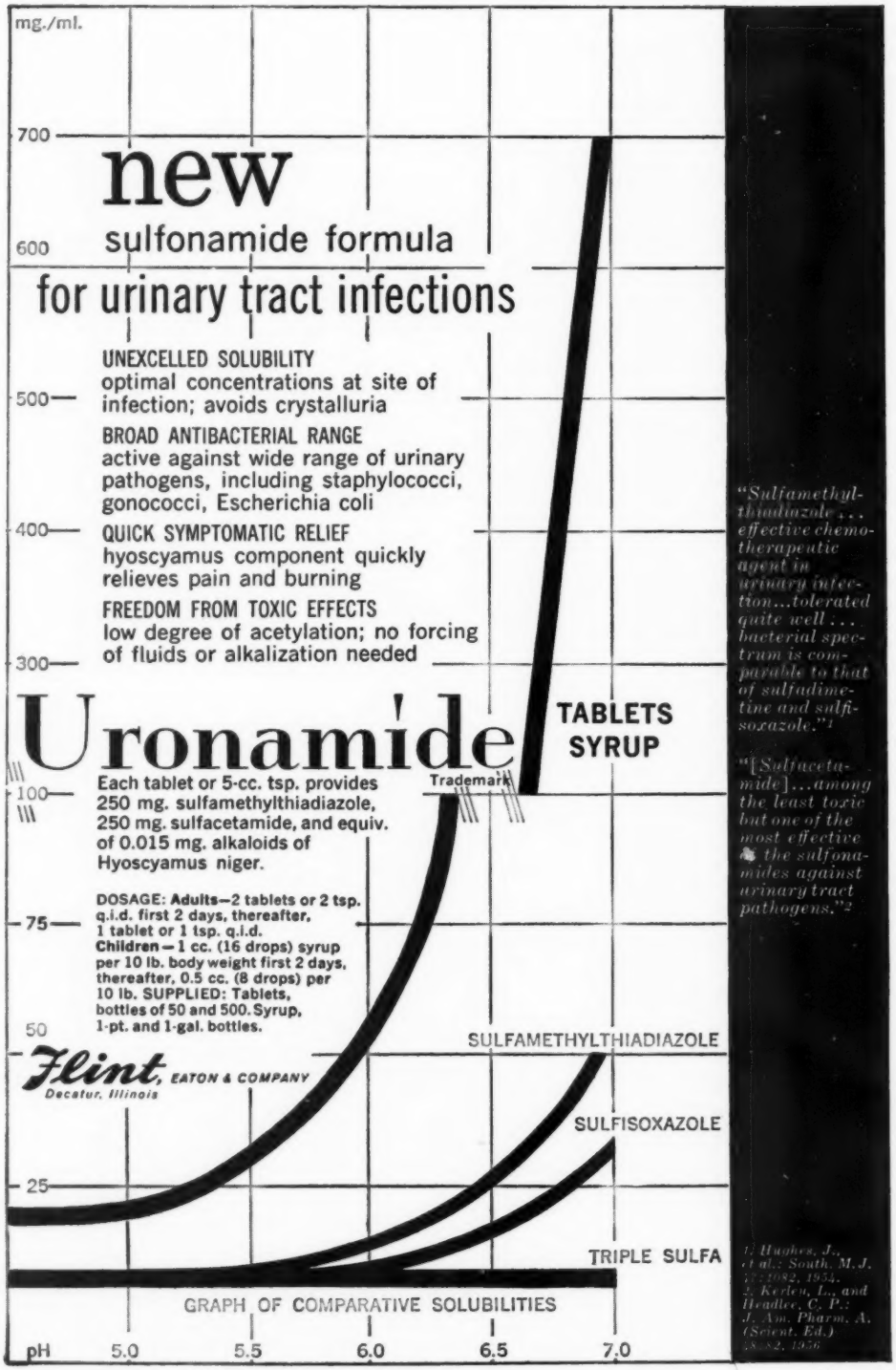


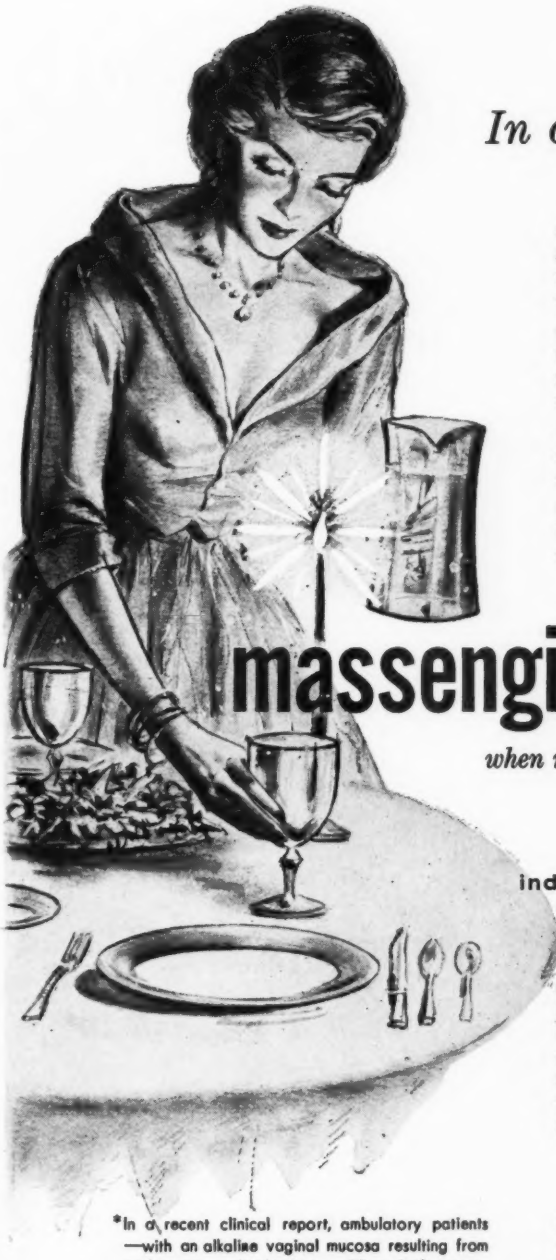
Wyeth
Philadelphia 1, Pa.

SUSPENSION TABLETS

SULFOSE®

Triple Sulfonamides
(Sulfadiazine, Sulfamerazine, Sulfamethazine)


mg./ml.
700
600
500
400
300
100
75
50
25
new
sulfonamide formula
for urinary tract infections
UNEXCELLED SOLUBILITY
optimal concentrations at site of infection; avoids crystalluria
BROAD ANTIBACTERIAL RANGE
active against wide range of urinary pathogens, including staphylococci, gonococci, Escherichia coli
QUICK SYMPTOMATIC RELIEF
hyoscyamus component quickly relieves pain and burning
FREEDOM FROM TOXIC EFFECTS
low degree of acetylation; no forcing of fluids or alkalization needed
Uronamide
Trademark
TABLETS
SYRUP
Each tablet or 5-cc. tsp. provides 250 mg. sulfamethylthiadiazole, 250 mg. sulfacetamide, and equiv. of 0.015 mg. alkaloids of Hyoscyamus niger.
DOSAGE: Adults—2 tablets or 2 tsp. q.i.d. first 2 days, thereafter, 1 tablet or 1 tsp. q.i.d.
Children—1 cc. (16 drops) syrup per 10 lb. body weight first 2 days, thereafter, 0.5 cc. (8 drops) per 10 lb. SUPPLIED: Tablets, bottles of 50 and 500. Syrup, 1-pt. and 1-gal. bottles.
Flint, EATON & COMPANY
Decatur, Illinois
SULFAMETHYLTHIADIAZOLE
SULFISOXAZOLE
TRIPLE SULFA
GRAPH OF COMPARATIVE SOLUBILITIES
pH 5.0 5.5 6.0 6.5 7.0
"Sulfamethylthiadiazole . . . effective chemotherapeutic agent in urinary infection . . . tolerated quite well . . . bacterial spectrum is comparable to that of sulfadimetine and sulfisoxazole."1
"[Sulfacetamide] . . . among the least toxic but one of the most effective of the sulfonamides against urinary tract pathogens."2
1. Hughes, J., et al.: South. M.J. 47:1082, 1954.
2. Kerlen, L., and Headley, C. P.: J. Am. Pharm. A. (Scient. Ed.) 45:52, 1956



In deference to her daintiness...

- Massengill Powder is buffered to *maintain** an acid condition in the vaginal mucosa. It is more effective than vinegar and simple acid douches.
- Massengill Powder has a low surface tension which enables it to penetrate into and cleanse the folds of the vaginal mucosa.
- Massengill Powder has a "clean" antiseptic fragrance. It enjoys unusual patient acceptance.
- Massengill Powder solutions are easy to prepare. They are nonstaining, mildly astringent.

massengill powder®

when recommending a vaginal douche

indications:

Massengill Powder solutions are a valuable adjunct in the management of monilia, trichomonas, staphylococcus, and streptococcus infections of the vaginal tract. Routine douching with Massengill Powder solution minimizes subjective discomfort and maintains a state of cleanliness and normal acidity without interfering with specific treatment.

*In a recent clinical report, ambulatory patients —with an alkaline vaginal mucosa resulting from pathogens—maintained an acid vaginal mucosa of pH 3.5 for 4 to 6 hours after douching with Massengill Powder; recumbent patients maintained a satisfactory acid condition up to 24 hours.

*Arnot, P.H.: West. J. Surg., Obs., and Gyn. 62:85

Generous samples on request.

The S. E. MASSENGILL Company

Bristol, Tennessee *New York* *Kansas City* *San Francisco*

no pai re

One DONNAGESIC Extentab gives 10 to 12 hours of steady, high-level codeine analgesia. Rebuilding of effective analgesia with repeated doses is avoided. Patient comfort is continuous.

There is more pain relief in DONNAGESIC Extentabs than in codeine alone—codeine analgesia is potentiated by the phenobarbital present. In addition, phenobarbital diminishes anxiety, lowering patient's reactivity to pain.

DONNAGESIC is safer, too, for codeine side effects are minimized by the peripheral action of the belladonna alkaloids.

extended action—The intensity of effects smoothly sustained all-day or all-night by each DONNAGESIC Extentab is equivalent to, or greater than, the maximum which would be provided by q. 4h. administration of one-third the active ingredients.

Donnagesic™ Extentabs*

extended action tablets of CODEINE with DONNATAL®

once and for all every 10-12 hours codeine uses

DONNAGESIC No. 1 (pink)		DONNAGESIC No. 2 (red)	
CODEINE Phosphate	48.6 mg. (¾ gr.)		97.2 mg. (1½ gr.)
Hyoscyamine Sulfate	0.3111 mg.		0.3111 mg.
Atropine Sulfate	0.0582 mg.		0.0582 mg.
Hyoscine Hydrobromide	0.0195 mg.		0.0195 mg.
Phenobarbital	48.6 mg. (¾ gr.)		48.6 mg. (¾ gr.)

A. H. ROBINS CO., INC., RICHMOND, VIRGINIA

Ethical Pharmaceuticals of Merit Since 1878

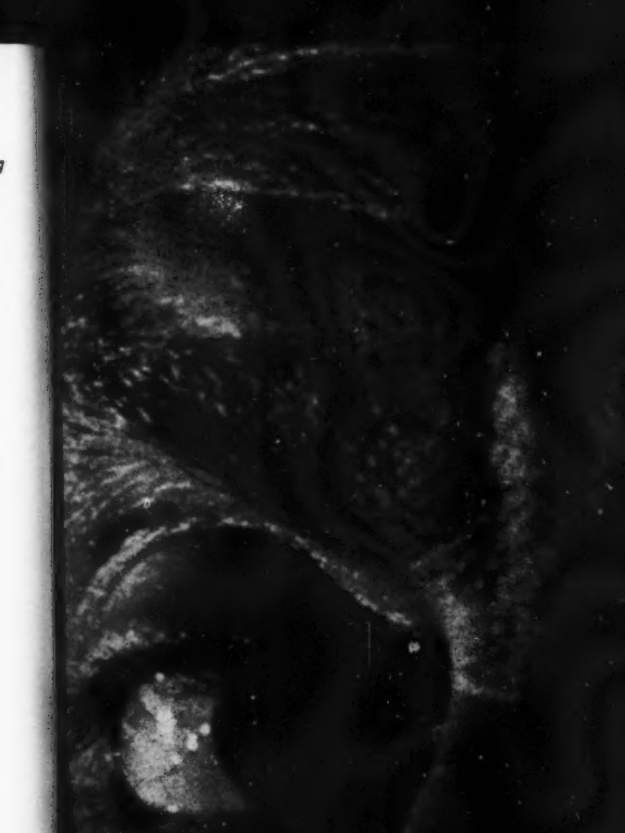
Robins

*Reg. U. S. Pat. Off., Pat. applied for.

Superficial skin complaints usually respond dramatically to TASHAN CREAM 'Roche'

Antipruritent, soothing, and healing—contains vitamins A, D, E, and *d*-Panthenol, in a cosmetically pleasing water-soluble base which fastidious patients will enjoy using. Hoffmann-La Roche Inc., Nutley, N. J.

TASHAN T. M.



external eye conditions consistently respond to...

Ophthalmic Suspension

(prednisolone acetate and sulfacetamide sodium)

Ointment with Neomycin

(prednisolone acetate and sulfacetamide sodium with neomycin sulfate)

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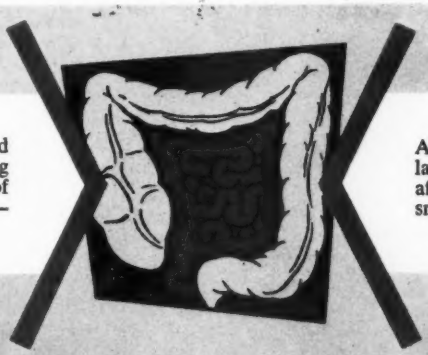

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1. Rezek, G. H.: Personal Communication; 2. Hannon, T. R.: Personal Communication; 3. Malleson J.: The Lancet, July 1953.

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The Natural History of Postnecrotic Cirrhosis*

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The clinical course, pathologic findings and management of postnecrotic cirrhosis are compared with those of portal cirrhosis.

IN COMPARISON WITH ALCOHOLIC AND CRYPTOGENIC PORTAL (LAENNEC'S) CIRRHOSIS, it has been noted that the bleeding and hypersplenism of postnecrotic cirrhosis freqently contraindicate liver biopsy and abdominal operation, that the response to medical treatment is unsatisfactory, and that hepatic parenchymal damage is invariably severe and often irreversible. In some quarters[1] the opinion is held that the clinical features of posthepatitic cirrhosis do not differ from those of portal cirrhosis. Marchand[2] in 1895, Mallory[3] in 1911, and Karsner[4] in 1943 were among the first to describe postnecrotic cirrhosis as multiple nodular hyperplasia, toxic cirrhosis or healed yellow atrophy. In 1952, Baggenstoss and Stauffer[5] compared clinically and pathologically a large series of cases of posthepatitic and alcoholic cirrhoses. Their classic presentation more clearly defined postnecrotic cirrhosis and re-emphasized that needle biopsy of the liver could not accurately classify this type of cirrhosis.

Material and Methods

Thirty unselected cases of postnecrotic cirrhosis, encountered at the Ochsner Clinic and Charity Hospital in New Orleans during the seven year period ending July 1, 1955, were studied to determine the clinical and morphologic features. These were proved by necropsy, in particular, by the presence of specific lobar or nodular areas of hepatic regeneration. None of the patients had primary biliary (cholangiolitic) cirrhosis. The results of this study were compared with those of a similar study of 30 unselected cases of portal (Laennec's) cirrhosis seen at these same institutions during the same period.

Twenty-six of the 30 patients with portal cirrhosis were men. The youngest patient was 37 years, the oldest 75 years, and the mean age 53 years at the time of the first examination. Ten of the 30 patients with postnecrotic cirrhosis were males. The youngest patient was 11 years, the oldest 72 years, and the mean age 41 years. Every patient with portal cirrhosis gave a history of alcoholism. Thirteen patients with postnecrotic cirrhosis had had a previous illness suggestive of infectious hepatitis. One patient had been exposed to carbon tetrachloride, and 16 had no significant etiologic record.

Clinical Data

Initial Signs or Symptoms. Abdominal pain, jaundice, peripheral edema and gastrointestinal hemorrhage were more prevalent initially in the clinical course of postnecrotic cirrhosis than in that of portal cirrhosis. Ascites was the commonest initial physical sign observed in patients with portal cirrhosis (Table 1).

Symptoms. Table 2 shows the incidence of symptoms in both types of cirrhosis. There did not appear to be any particular difference in the symptoms whether the diagnosis was made at the time of liver biopsy or terminally. The only significant variations in the incidence of symptoms in both groups were

*Read before the Section on Gastroenterology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

†From the Department of Gastroenterology, Ochsner Clinic and the Department of Medicine, Tulane University School of Medicine, New Orleans, La.

TABLE 1

INITIAL CLINICAL MANIFESTATIONS IN 30 CASES EACH OF POSTNECROTIC AND PORTAL CIRRHOSIS

Initial Manifestations	*Cirrhosis*	
	Postnecrotic Cases	*Portal Cases*
Jaundice	13	4
Abdominal pain	9	6
Edema	7	5
Gastrointestinal hemorrhage	4	2
Ascites	2	11
Fever	1	0
Nausea / vomiting	1	0
Dyspnea	0	2
Fatigue	0	2
Neuritis, pruritus, hemorrhoids, anorexia, indigestion	0	1 each

the presence of abdominal pain, menstrual irregularities and pruritus in patients with postnecrotic cirrhosis.

Physical Signs. Table 3 illustrates the incidence of physical findings in portal and postnecrotic cirrhosis. Splenomegaly, edema, ascites, endoscopic evidence of esophageal varices, fever, loss of hair, gynecomastia, testicular atrophy and striae were noted more frequently in patients with both types of cirrhosis late in the clinical course than at the time of liver biopsy. Jaundice was usually a late clinical manifestation of portal cirrhosis occurring terminally in 12 cases. Ascites and edema were commoner in portal cirrhosis. The palpable liver was larger in portal cirrhosis, and larger spleens were palpated in postnecrotic cirrhosis. Hypersplenism occurred in 14 cases of postnecrotic cirrhosis and 3 cases of portal cirrhosis.

Laboratory Data. The significant laboratory data in both groups of cirrhosis are listed in table 4. Hypersplenism was observed more frequently in patients with postnecrotic cirrhosis. In these patients leukopenia, thrombocytopenia, normocytic anemia, reticulocytosis, elevation of the indirect serum bilirubin, normoblastic hyperplasia of the bone marrow, increased fecal and urinary urobilinogen values, and hemosiderosis of the liver and spleen, which are seen wholly or in part as manifestations of secondary hypersplenic states, were observed. The incidence of hyperglobulinemia, abnormalities of hepatic flocculation tests, hypoprothrombinemia, hyperbilirubinemia, and low values for the plasma

TABLE 2

COMPARISON OF EVENTUAL SYMPTOMS IN 30 CASES EACH OF POSTNECROTIC AND PORTAL CIRRHOSIS

Symptom	*Postnecrotic Cases*	*Portal Cases*
Weakness	30	30
Abdominal pain	22	18
Gastrointestinal hemorrhage	19	9
Bleeding tendency	16	5
Menstrual irregularities	10	0
Dyspnea	8	12
Nausea	5	8
Vomiting	4	8
Diarrhea	4	6
Pruritus	4	2

TABLE 3

COMPARISON OF PHYSICAL SIGNS IN 30 CASES EACH OF POSTNECROTIC AND PORTAL CIRRHOSIS

Physical Signs	*Cirrhosis*	
	Postnecrotic Cases	*Portal Cases*
Enlarged liver	22	27
Enlarged spleen	21	18
Esophageal varices (esophagoscopy)	19	18
Jaundice	18	3
Edema	15	21
Spider angioma	12	20
Ascites	12	17
Fever	12	5
Ecchymosis	9	2
Palmar erythema	8	18
Paracentesis	7	14
Alopecia	5	15
Striae	4	8
Gynecomastia	2	5
Testicular atrophy	2	7
Clubbing of fingers	1	2
Caput medusae	0	1

TABLE 4

COMPARISON OF LABORATORY DATA IN 30 CASES EACH OF POSTNECROTIC AND PORTAL CIRRHOSIS

Laboratory Data	*Cirrhosis*	
	Postnecrotic Cases	*Portal Cases*
Leukopenia	16	7
Leukocytosis	1	9
Thrombocytopenia	21	14
Anemia	8	12
Hyperglobulinemia	8	18
Abnormal cephalin-flocculation	18	15
Abnormal thymol turbidity	27	17
Abnormal zinc sulfate	8(8)*	7(7)
Low serum cholinesterase	3(4)	4(4)
Hypoprothrombinemia	22	5
Elevation serum iron	4(4)	3(4)
Positive blood serology	2	2
Low cholesterol-cholesterol esters	14	8
Average BSP (45 minutes)	33	21
Average sedimentation rate (Westergren)	36	48
Average direct serum bilirubin	2.6	1.4
Average total serum bilirubin	6.7	3.1

*Numbers in parentheses indicate limited number of cases studied.

TABLE 5

MEAN ELECTROPHORETIC VALUES OF THE SERUM PROTEINS IN CIRRHOSIS
(Grams per 100 cc. blood)

A/G Ratio	*Albumin*	*Globulin Alpha 1*	*Globulin Alpha 2*	*Beta Globulin*	*Gamma Globulin*
Normal Serum 1:1-1.7	3.8-4.6	0.2-0.5	0.5-1.2	0.75-1.3	1.1-1.7
Portal Cirrhosis 0.8	3.0	0.2	0.5	0.9	2.3
Postnecrotic Cirrhosis 0.3	1.5	0.53	0.69	1.44	3.15

cholesterol-cholesterol esters was greater in postnecrotic cirrhosis. Two patients with postnecrotic cirrhosis had interesting laboratory data. In one the results of hepatic flocculation tests were minimally abnormal and the bromosulphonphthalein retention was zero at 45 minutes. In the other, hypergammaglobulinemia was determined electrophoretically.[6] The results of plasma electrophoresis in 8 patients with both types of cirrhosis are listed in table 5.

Pathologic Data

Eleven patients with postnecrotic cirrhosis and 8 with portal cirrhosis died of hepatic insufficiency. Death from bleeding esophageal varices occurred in 4 patients with postnecrotic cirrhosis and in 5 with portal cirrhosis. A hepatoma and postoperative pneumonia, respectively, accounted for deaths in 2 patients with portal cirrhosis.

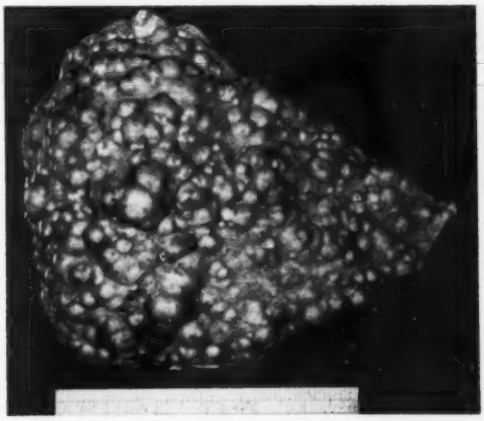
The mean weights of the liver and spleen, respectively, were 2,325 grams and 550 grams in the patients with portal cirrhosis and 1,150 grams and 405 grams in those with postnecrotic cirrhosis. The gross appearance of the size and distribution of the regenerative nodules was studied, and the livers were classified into three groups according to the study of Baggenstoss and Stauffer.[5] Extremely large regenerative nodules and distortion of the hepatic contour were found in 9 patients with postnecrotic cirrhosis (Fig. 1), and were called the lobar group. The nodular group, in which the remainder of the livers of postnecrotic cirrhosis were classified, had the characteristics of more evenly distributed and smaller regenerative nodules than the lobar group (Fig. 2). All livers from patients with portal cirrhosis fell into the granular group (Fig. 3). In these cases the regenerative nodules are small and the zones of fibrosis are narrow.

Histologically, postnecrotic cirrhosis was characterized by,—(1) variable sized (larger than 1 cm.) regenerative nodules containing round cells, atypical hepatic cells, no alcoholic-hyalin and extensive focal necrosis, and (2) wide zones of fibrous connective tissue containing round cells, distorted reticulum fibers, and compression of large venules (Fig.

FIG. 1

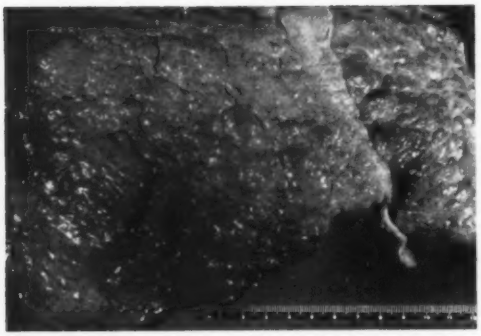
Postnecrotic cirrhosis (lobar type). Large regenerative nodules. Atrophic liver, weight 1,200 Gm. Broad areas of fibrosis.

FIG. 2



Postnecrotic cirrhosis (nodular type) in girl 17 years old. Regenerative nodules measuring 1.5 cm. in diameter. Atrophic liver, weight 918 Gm.

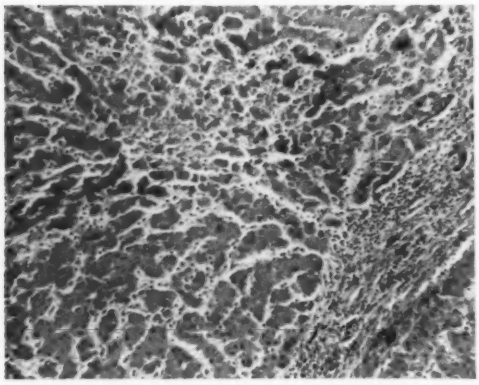
FIG. 3



Portal cirrhosis in patient with alcoholism aged 65 years. Classic granular regenerative nodules, uniform size, measuring 0.3 to 0.5 cm. in diameter. Liver weight 2,250 Gm.

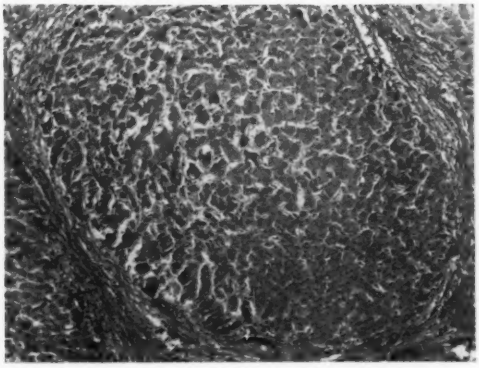
4). Mechanically, a small needle biopsy may not secure sufficient tissue from the large-sized regenerative nodules in postnecrotic cirrhosis. Therefore, tissue obtained by needle biopsy of the liver may not satisfy the histologic criterion of cirrhosis, which is nodular regeneration, fibrosis and hepatic cellular necrosis. In 7 patients with postnecrotic cirrhosis the histologic diagnosis of hepatic tissue obtained by needle biopsy was hepatitis; in 5 of these sufficient phases were present to suspect cirrhosis; in 3 nodular regeneration was recognized. Fatty infiltration of the liver so commonly seen in alcoholic portal cirrhosis was not identified in livers of the postnecrotic group. All the histologic features of portal cirrhosis were recognized in the group with Laennec's cirrhosis (Fig. 5).

FIG. 4



Postnecrotic cirrhosis. Incomplete regenerative nodule, wide internodular stroma, severe hepatic necrosis, no fatty infiltration, balloon-cells (X 80).

FIG. 5



Portal cirrhosis. Small regenerative nodules, narrow internodular stroma, mild hepatic cell necrosis. Fatty infiltration compression of central vein (X 80).

Medical Management

Many forms of medical therapy were administered including the Patek diet,[7] restriction of sodium intake, lipotropic substances, intravenous administration of glucose and vitamins, transfusions of whole blood, administration of liver extract, antibiotics, mercurials, corticotropin, cortisone, intravenous administration of sodium glutamate, repeated paracenteses and oxygen therapy. Various surgical procedures were done for esophageal hemorrhage, such as portacaval shunt, esophagogastrectomy, ligation of the hepatic artery and splenectomy. The results of medical and surgical treatment and survival rates will be the subject of a larger series of cases of cirrhosis in another investigation.[8]

Generally, survival rates of patients with portal cirrhosis following the onset of ascites, jaundice and the initial bout of hematemesis were similar to those reported by Ratnoff and Patek[9] and Fleming and Snell.[10] Similarly, the survival rates of patients with postnecrotic cirrhosis with these clinical findings disclosed that the number of patients alive during a seven year period was much less than that of the group with portal cirrhosis.

Comment

This investigation suggests, as others have, that postnecrotic cirrhosis is a posthepatitic cirrhosis, because its large, irregular regenerative nodules are probably evidence of pronounced hepatic regeneration after virulent hepatitis. A history of hepatitis was elicited

in 43 per cent of the patients with postnecrotic cirrhosis.[11] This type of cirrhosis was found more frequently in females and in a younger age group than was portal cirrhosis. Patients with postnecrotic cirrhosis had not only a more progressive clinical course despite any type of therapy but also more severe hepatic cellular damage than those with portal cirrhosis. Hepatic pain, jaundice, edema, menstrual irregularities, pruritus, bleeding phenomenon, hypersplenism, intercurrent infection, larger spleens and smaller livers were more frequently observed in postnecrotic cirrhosis than in portal cirrhosis. Abnormalities of protein synthesis, hypergammaglobulinemia, abnormal results of hepatic flocculation tests, low cholesterol esters, hypoprothrombinemia, leukopenia, and thrombocytopenia characterized significant abnormal laboratory data in the postnecrotic group. Finally, hepatic insufficiency was the most common cause of death in postnecrotic cirrhosis. These clinical and biochemical findings emphasize the intensity and progression of hepatic inflammation in postnecrotic cirrhosis, as compared with more pronounced manifestations of portal hypertension in those with Laennec's cirrhosis. Pathologically, a normal sized or atrophic liver with lobar or nodular areas of regeneration characterized postnecrotic cirrhosis. Larger livers with granular hepatic regeneration are seen in portal cirrhosis. Histologically, as Baggenstoss and Stauffer[5] stated, and this study confirms, postnecrotic cirrhosis discloses active hepatitis, severe hepatocellular necrosis, wide zones of fibrosis, round cell infiltration, and compression of large veins. In addition, the large sized regenerative nodules of postnecrotic cirrhosis escape complete identification histologically in needle biopsy specimens. The smaller regenerative nodules of portal cirrhosis, which compress a greater number of smaller hepatoportal venules, may explain the higher incidence of portal hypertension in those with portal cirrhosis. This study did not include posthepatitic or cryptogenic portal cirrhosis in which the regenerative nodules are granular in size.[12-14] Postnecrotic cirrhosis is characterized pathologically by lobar or nodular areas of hepatic regeneration which may be a sequela of viral or toxic hepatitis,[15-17] and clinically by severe hepatic insufficiency.[18]

The results of medical treatment and operation for hypersplenism and portal hypertension have been poorer in postnecrotic cirrhosis than in portal cirrhosis. Survival curves clearly show the poorer prognosis of postnecrotic cirrhosis in comparison with portal cirrhosis, particularly after the initial onset of jaundice, ascites or hematemesis.

Conclusion

A clinical and pathologic study of postnecrotic and alcoholic portal cirrhoses has shown that physical and laboratory signs of hepatocellular insufficiency dominate the postnecrotic group and those of portal hypertension characterize portal cirrhosis.

Large regenerative nodules together with active hepatic degeneration are the main pathologic observations in postnecrotic cirrhosis.

The response of postnecrotic cirrhosis to medical or surgical treatment is invariably poorer than that of portal cirrhosis.

Information derived from the survival curves of both types of cirrhosis emphasizes the poorer prognosis of postnecrotic cirrhosis.

References

1. Sherlock, S.: Diseases of the Liver and Biliary System, Springfield, Illinois, Charles C. Thomas, Publisher, 1955.
2. Marchand, F.: Ueber Ausgang der acuten Leberatrophie in multiple Knotige Hyperplasie, Beitr. path. Anat. 17:206, 1895.
3. Mallory, F. B.: Cirrhosis of the Liver; Five Different Types of Lesions from Which It May Arise, Bull. Johns Hopkins Hosp. 22:69, 1911.
4. Karsner, H. T.: Morphology and Pathogenesis of Hepatic Cirrhosis, Am. J. Clin. Path. 13:569, 1943.
5. Baggenstoss, A. H., and Stauffer, M. H.: Posthepatitic and Alcoholic Cirrhosis; Clinicopathologic Study of 43 Cases of Each, Gastroenterology 22:157, 1952.
6. Bearn, A. G., Kunkel, H. G., and Slater, R. J.: The Problem of Chronic Liver Disease in Young Women, Am. J. Med. 21:3, 1956.
7. Patek, A. J., Jr., and Post, J.: Treatment of Cirrhosis of the Liver by a Nutritious Diet and Supplements Rich in Vitamin B Complex, J. Clin. Invest. 20:481, 1941.
8. Kleckner, M. S., Jr.: Cirrhosis of the Liver—A Clinical Presentation, Springfield, Illinois, Charles C. Thomas, Publisher. (In preparation).
9. Ratnoff, O. D., and Patek, A. J., Jr.: The Natural History of Laennec's Cirrhosis of the Liver, Medicine 21:207, 1942.
10. Fleming, R. G., and Snell, A. M.: Portal Cirrhosis with Ascites, Am J. Digest. Dis. 9:115, 1942.
11. Howard, R., and Watson, C. J.: Antecedent Jaundice in Cirrhosis of the Liver, Arch. Int. Med. 80:1, 1947.
12. Sherlock, S.: Post-hepatitis Cirrhosis, Lancet 1:817, 1948.
13. Kosalka, M. F., Lindert, M. C. F., Snodgrass, H. M., and Lerner, H. B.: Hepatitis and Its Sequelae Including the Development of Portal Cirrhosis, Arch. Int. Med. 84:782, 1949.
14. Perkins, R. F., Baggenstoss, A. H., and Snell, A. M.: Viral Hepatitis as a Cause of Atrophy and Cirrhosis of the Liver, Proc. Staff. Meet. Mayo Clin. 25:287, 1950.
15. Stine, L. A., and Swarts, J. M.: Postnecrotic (toxic) Cirrhosis; Its Clinical Significance, Am. J. Digest. Dis. 19:176, 1952.
16. Pratt, J. H., and Stengel, A.: Toxic Cirrhosis Resulting from Acute Liver Atrophy, Am. J. M. Sc. 173:1, 1927.
17. Bjorneboe, M., and Raaschou, F.: Pathology of Subchronic Atrophy of the Liver, Arch. Int. Med. 84:933, 1949.
18. Ratnoff, O. D., and Patek, A. J., Jr.: Postnecrotic Cirrhosis of the Liver, J. Chronic Dis. 1:266, 1955.

Portal Hypertension as Assessed by Hepatic Venule Catheterization*

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Catheterization of the hepatic venule to determine the pressure in the portal system can be used to predict the success or failure of portacaval shunt operations.

Introduction

GASTROINTESTINAL HEMORRHAGE, ASCITES, HEPATIC INSUFFICIENCY AND HYPERSPLENISM are the principal motivating factors which stimulate the clinical appraisal of portal pressure.

The portal vein receives the splenic vein and the superior mesenteric veins, and since the portal system is a valveless one, the pressures in one part of the system should be transmitted throughout. Meyers and Taylor,[1] and more recently Paton[2] and associates, assessed portal pressure by occlusive catheterization of the hepatic venule in normal persons and in patients with portal hypertension. Recent and current studies have been performed confirming this as a practical reliable method of measuring portal pressures.

Methods

Simultaneous pressure determinations were made in the hepatic venule and portal vein in portal normotensive and portal hypertensive individuals. Saline manometric pressures were read from a point 9 cm. above the posterior chest wall in the reclining position. In the early part of this study occlusive pressures in the hepatic venule were first obtained in the preoperative state. The patients were then moved to the operating room with the catheter in the hepatic venule where, under general endotracheal ether anesthesia, the abdomen was opened and simultaneous pressure determinations were made directly in the portal vein or one of its tributaries, and again in the hepatic venule through the previously introduced catheter.

With the validity of the method established, observations were made on the effect of maximum forced expiration against the closed glottis (Valsalva) in patients with cirrhosis, and for variable periods of time after portacaval shunts.

Results

Nineteen patients were studied employing the occlusive catheterization technic. The normal hepatic venule pressure with this method is 12 to 22 cm. of normal saline.

Simultaneous observations of pressure in the hepatic venule and portal vein were made in 10 subjects and the coefficient of correlation between the two pressure sites has been found to be 0.87 ± 0.77. The linear distribution of these results is graphically represented in figure 1. In all but one case there was a consistent rise (as much as 17 cm. in some instances) in the hepatic venule pressure at the time of operation. This may be the result of mild shock or even due to activation of functional hepatic arteriovenule shunts.[3]

The forced Valsalva resulted in a temporary pressure rise of 60 to 70 cm. of saline in the occluded hepatic venule in normal subjects and in patients with cirrhosis. By contrast, pressures obtained by direct needling of esophageal varices are reported to rise no more than 25 to 30 cm. of normal saline with the Valsalva maneuver.[4]

Further analysis of these cases reveals two general groups, the portal normotensive and the portal hypertensive (Tables 1 and 2).

*Read before the Section on Gastroenterology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

†From the Departments of Medicine and Surgery, Tulane University School of Medicine and the Louisiana State University School of Medicine, and the Browne-McHardy Clinic, New Orleans, La.

TABLE 1

PORTAL NORMOTENSIVE GROUP

Diagnosis	*Cases*	*Pressure in Cm. Normal Saline*
1. No Hepatoportal disease	6	12-22
2. Biliary cholangitis	1	19
3. Metastatic carcinoma of liver	2	20-21
4. Carcinoma of liver and splenomegaly	1	21
5. Hemangiomata with splenomegaly	1	12
6. Rheumatic heart disease Splenomegaly and hematemesis	1	15
7. Gastritis with hepatomegaly and hematemesis	1	17

Cases 5, 6 and 7 presented themselves with massive upper gastrointestinal hemorrhages. Preoperative catheterization studies revealed normal pressure, and it was not until operation that a definitive diagnosis was established.

Portal hypertension, hemorrhage and splenomegaly are the most common findings in Group 2 (Table 2). In no instance was bleeding produced by raising the portal pressure 60 to 70 cm. of normal saline, suggesting that additional factors (local and systemic) are necessary before hemorrhage occurs.

Similarly portal hypertension is but one of the factors responsible for ascites formation in cirrhotics.

Surgical decompressing procedures such as portacaval shunts and splenorenal shunts are directed at reducing portal pressure; thus when pressure is normal or only slightly elevated little relief may be anticipated.

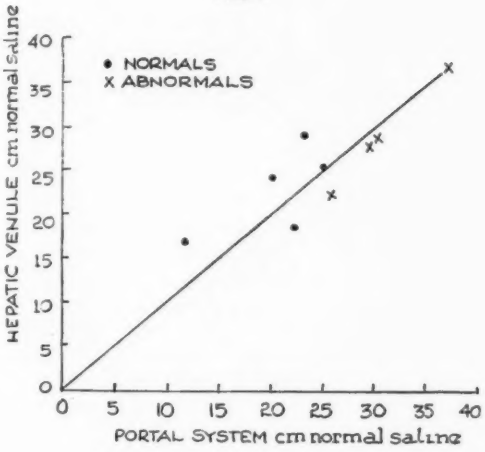
It is in the selection of these patients that the occlusive catheterization technic may be helpful since operations of this type in the face of a relatively normal portal pressure would be useless.

TABLE 2

PORTAL HYPERTENSIVE GROUP

Diagnosis	*Cases*	*Pressure in Cm. Normal Saline*
Cirrhosis	6	27-34
Clinical	Frequency	
Splenomegaly	6	
Hemorrhage	5	
Small liver	2	
Ascites	2	
Hepatomegaly	4	

FIG. 1



(Courtesy Am. J. M. Sc. 228:643, 1954)

Conclusions

1. The method of occlusive catheterization of the hepatic venule is a valid way of assessing portal pressure.

2. It may aid in the location of the site of portal obstruction either intra- or extrahepatic.

3. The forced Valsalva maneuver produces a rise of 60 to 70 cm. of normal saline in normal subjects and in patients with liver disease.

4. The selection of patients for portacaval shunt may be facilitated since there is a small group that may have ascites, relatively good liver function, and no hemorrhage, and may benefit from the shunt procedure provided significant portal hypertension is present.

5. This technic may be used to follow the postoperative course of cases of portacaval shunt regarding the patency of the shunt.

References

1. Meyers, J. D., and Taylor, W. J.: An Estimation of Portal Venous Pressure by Occlusive Catheterization of an Hepatic Venule, J. Clin. Invest. 30:662, 1951.
2. Paton, A., Reynolds, T. B., and Sherlock, Sheila: Assessment of Portal Venous Hypertension by Catheterization of Hepatic Vein, Lancet 1:918, 1953.
3. Welch, G. E., Emmett, R., Craighead, C. C., Hoeffler, G., Browne, D. C., and Rosen, I.: Simultaneous Pressure Measurements in Hepatic Venule and Portal Venous System in Man, Am. J. M. Sc. 228:643, 1954.
4. Palmer, E. D.: Effect of Valsalva Maneuver on Portal Hypertension in Cirrhosis, Am. J. M. Sc. 227:661, 1954.

Acute Thrombosis of the Portal Vein*

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The authors report a case successfully managed by the use of anticoagulants.

ACUTE THROMBOTIC OCCLUSION of the portal vein is a comparatively uncommon disorder, and generally is regarded as universally fatal. Most of the literature on the subject is comprised of isolated case reports, the majority of authors dealing with the chronic form which is more amenable to treatment. Our purpose is to review the subject of acute thrombosis of the portal vein from its etiologic, pathophysiologic and clinical aspects. We shall suggest a form of therapy which may prove beneficial in certain instances. A case illustrating the successful application of this program will be presented, with a summary of the patient's status following a two year interval.

Anatomy and Physiology of the Portal Vein

The portal vein is unique among the regional circulatory vessels in that it is situated between two capillary beds, those of the gastrointestinal tract and spleen on the one hand and those of the hepatic parenchyma on the other. The structure is formed by the union of the superior mesenteric vein with the splenic vein, the inferior mesenteric vein usually flowing into the latter structure. Originating at the level of the second lumbar vertebra, in front of the vena cava and behind the neck of the pancreas, it ascends behind the superior portion of the duodenum, thence in the right border of the lesser omentum to the porta hepatis. Here it divides into a right and left branch to enter the substance of the liver.[1,2] The portal vein drains the digestive tract from the stomach to the proximal portion of the rectum, and the spleen; the splenic vein contributes 20 to 40 per cent of the total portal blood flow.[3] Products of digestion, absorbed into the mesenteric vessels, are transported to the liver by the portal vein for metabolic processing.

Total hepatic blood flow is estimated at 1,500 to 2,000 cc. per minute, of which approximately 75 per cent is contributed by the portal system.[3,4] A definite reciprocal relationship exists between the hepatic arterial flow, and that of the portal vein. Pressures within the portal system average 10 to 12 cm. of saline above the right auricle.[5-8] Portal vein blood has a higher oxygen and glucose content than the hepatic vein or the vena cava; the content of protein, urea, sodium, potassium, chloride, calcium, and phosphorus are essentially identical in the portal vein, hepatic vein, hepatic artery, and peripheral vessels.[5,9]

It has long been known that the liver can survive deprivation of its portal blood supply. The Eck fistula animal, as well as the animal with mechanical portal occlusion, maintains life by means of hepatic arterial blood.[10] Humans have also been found capable of tolerating sudden complete and permanent interruption of portal flow by surgical means.[11]

Collateral Circulation

The portacaval shunt system used by blood from the digestive tract following portal vein obstruction is well known. This hepatofugal system is listed in table 1.[2] Less well known is the hepatopetal system,[12] through which

TABLE 1

HEPATOFUGAL COLLATERAL CIRCULATION*

1. Superior hemorrhoidal vein (portal) to middle and inferior hemorrhoidal veins (caval).
2. Veins along ligamentum teres (portal) via para-umbilical veins to superior and inferior epigastric veins (caval).
3. Retroperitoneal veins of Retzius (portal) to renal and lumbar veins (caval).
4. Sappey's veins from bare area of liver (portal) to diaphragmatic veins (caval).
5. Coronary vein of stomach (portal) to the esophageal plexus (caval via azygos).

*DeGaris and Portis[2]

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TABLE 2

HEPATOPETAL COLLATERAL CIRCULATION

Anastomoses between the portal vein and:

1. Deep cystic veins.
2. Epiploic veins of the lesser omentum, hepatocolic and hepatorenal ligaments.
3. Veins of hilum of the liver, vasa vasorum of portal vein and hepatic artery, and veins in the wall of the common bile duct.
4. Diaphragmatic veins.
5. Veins in the suspensory ligaments of the liver.
6. Para-umbilical veins.

mesenteric blood can still reach the liver despite a block in the portal bed (Table 2). Spontaneous portacaval shunts have been repeatedly demonstrated in individuals without disease of the portal vein. Apparently these anastomoses are easily opened.[13] Following portal vein thrombosis both systems are called into play.

Incidence and Etiology of Acute Thrombosis of Portal Vein

This lesion is relatively uncommon, occurring in approximately 0.35 per cent of autopsies. Lissauer[14] encountered acute thrombosis of the portal vein in 68 of 26,687 postmortem examinations; Webster[15] found 21 cases in a series of 6,050 autopsies. A survey of autopsy reports from the Mississippi Baptist Hospital and the Veterans Administration Hospital of Jackson revealed an over-all incidence of 0.42 per cent.

The disorder appears nearly twice as frequently in males as in females, probably because of the higher incidence among men of hepatic cirrhosis, the most common etiologic factor. Males develop the disease at an average age of 44.8 years, females at a median of 41 years.[16]

Hepatic cirrhosis and intra-abdominal malignancy are the two most common causes of thrombosis of the portal vein. A host of other etiologic conditions have been documented in such excellent reviews as those of Lichtman,[16] Bockus,[17] Johnson,[18] Kelsey,[19] and Simonds.[20] Table 3 summarizes the various pathologic states which may result in pylethrombosis.

Pathology

Clots in acute thrombosis are soft, usually hemorrhagic, and loosely attached to the vessel wall. The vein is distended at the area of thrombosis and may be dilated proximally. Occasionally the clot is placed parietally only incompletely obstructing the lumen. In such instances splenomegaly rarely develops. The thrombus may totally block the vein in one region and incompletely in another; the center of the clot may remain patent. The clot may be confined to the main body of the portal vein or it may extend into one or more of the intrahepatic ramifications.[16,21] Thrombotic propagation into the various portal tributaries does not necessarily develop; however, involvement of the mesenteric veins with subsequent hemorrhagic infarction of the intestine is the usual sequence and the common cause of exitus.[16,17,20]

Various alterations occur in the intra-ab-

TABLE 3

ETIOLOGY OF ACUTE PORTAL VEIN THROMBOSIS

I. Changes in the composition of the blood
   - A. Polycythemia vera
   - B. Thrombocythemia
   - C. Idiopathic migratory thrombophlebitis (?)

II. Portal vein stasis
   - A. Intrahepatic
     1. Portal cirrhosis
     2. Hepatic malignancy
     3. Hepatic syphilis
     4. Abscess, cysts, and other hepatic tumors
     5. Hepatic vein occlusion
     6. Congestion of liver due to caval compression above orifices of hepatic veins.
        - a. Pericarditis
        - b. Congestive heart failure
        - c. Tricuspid stenosis
   - B. Extrahepatic
     1. Periportal lymphadenopathy
        - a. Inflammatory
        - b. Malignant
     2. Gastric carcinoma
     3. Pancreatic carcinoma
     4. Cholecystic or choledochal disease
        - a. Inflammatory
        - b. Neoplastic
        - c. Lithiasis
     5. Portal fissure adhesions
     6. Peritonitis

III. Affections of the portal vein
   - A. Primary
     1. Phlebosclerosis
     2. Syphilis
   - B. Secondary
     1. Following any of the causes of suppurative pylephlebitis
     2. Following systemic infections
     3. Following abdominal trauma
     4. Following splenectomy

IV. Extension of thrombus, infection, or neoplastic process to portal vein from adjacent structures or via portal vein tributaries.
   - A. Splenic vein thrombophlebitis
   - B. Mesenteric vein thrombophlebitis
   - C. Carcinoma of liver or bile ducts
   - D. Carcinoma of other intra-abdominal organs; pancreas, stomach, colon, etc.

V. Idiopathic

dominal organs following pylethrombosis. The liver, unless already the site of carcinoma or cirrhosis, is less affected than might be expected. The hepatic artery and its branches are usually dilated, reciprocal to the diminished portal flow. Fatty changes in the parenchymal cells may develop. Occasionally infarcts are observed.[20] Splenomegaly develops in proportion to the degree of occlusion of the portal vein. Unless a significant degree of obstruction accompanies the thrombosis, the degree of splenic congestion is insufficient to produce enlargement. In complete portal block the spleen rapidly becomes more prominent.[16,20] The pancreas presents numerous changes. Fat necrosis, fibrosis, various degrees of pancreatitis, and thrombosis of the pancreatic veins have been found singly or in combination.[16,20,21] The small intestine is involved if the thrombus propagates into the mesenteric veins. Hemorrhagic infarction, commonly situated in the jejunum, proceeding to gangrene, is the lethal consequence of such a development.[16-18] The hepatopetal and hepatofugal collateral circulatory systems (Tables 1 and 2) are immediately utilized commensurate with the degree of portal block; venous engorgement of the entire gastrointestinal tract results from the back pressure.[22,23]

Pathophysiology

Hepatic function may not be seriously impaired. If the portal block is complete and should the hepatopetal collaterals be insufficiently patent, some impairment of hepatic integrity may be expected.[16] With intrahepatic portal thrombosis, more extensive damage will become apparent; in such instances jaundice may develop.[24] Pancreatic damage may be of sufficient degree to produce alimentary glycosuria and impaired glucose tolerance.[20] Gastrointestinal vascular stasis and engorgement are reflected in diarrhea, distention, and flatulence.[25] Transport of ingested glucose via collaterals "around" the liver may also produce glycosuria.[26] Pain results from the clot in the portal vein, but is also produced by swelling of the spleen and engorgement of the collateral circulation.[23] Where infarction occurs, melena, shock, and even hematemesis are present.[17] Ascites, which may accumulate rapidly, is the result of increased pressure within the portal system.[27] Although we are aware of no manometric studies in cases of acute pylethrombosis, it would seem likely that values exist which are of the same order as those found in other types of portal hypertension. These pressures usually well exceed 20 cm. of saline.[6-8,22] The manifestations of hypersplenism and bleeding varices, commonly encountered in chronic portal thrombosis, do not have time to develop in the acute type since death closes the scene too quickly.

The Clinical Picture

Clinical Signs and Symptoms. It should be borne in mind that the picture of acute thrombosis of the portal vein rarely arises *de novo,* but is usually superimposed upon some preexisting pathologic process. For this reason the classical manifestations rarely appear in a "pure" form. The site, severity, and extent of the thrombus also determine the clinical manifestations. The following appear in various combinations subsequent to acute clot formation:

(1) Pain, which is moderate to severe, sudden in onset, and steady or colicky in nature. The distress is felt in the right upper quadrant or epigastrium, and is frequently referred to the back. Gallbladder colic may be mimicked exactly. Nausea and vomiting are common.[16,17,28]

(2) Ascites. The fluid may be obvious, or may be discovered only at laparotomy or postmortem examination. Rapidly re-accumulating ascites following paracentesis is commonly observed. Ascites does not appear in all cases, particularly in those with efficient collateral circulations.[20,25]

(3) Splenomegaly, of minimal to moderate degree.[16,17,25,26]

(4) Diarrhea.[25]

(5) Melena, ileus, hematemesis, shock, and terminal coma.[16,17,20]

Once gastrointestinal thrombosis develops, the course is relentlessly downhill to exitus.

Laboratory Findings. Various degrees of impairment will be found in the profile of liver function tests, but there is no diagnostic pattern common to pylethrombosis. Some degree of bromsulphalein retention may be expected.[17] Glycosuria, impaired glucose tolerance, and elevated serum amylase reflect pancreatic dysfunction.[20] The gallbladder commonly fails to be visualized.[17,28] Roentgen studies of the gastrointestinal tract may ap-

pear to be perfectly normal. Alterations in the appearance of the jejunum have been described following propagation of the thrombus into the mesenteric veins.[29]

Treatment

It has been stated that acute thrombosis of the portal vein is uninfluenced by therapy,[17] the process advancing to intestinal thrombosis and death. The average duration of life is 6 to 8 days.[18] One should realize that death comes not from the portal vein thrombosis *per se*, nor from interruption of portal blood flow, but rather from the complications arising from propagation of the clot, usually intestinal thrombosis. Even if the condition responsible for thrombus formation is a potentially fatal disorder, by preventing these complications life can at least be prolonged; should the cause be benign, life may be saved. It would appear that anticoagulant therapy, begun early in the course of the disease would be an ideal and logical form of management. Luke[30] reported a case of mesenteric thrombosis successfully treated by the intravenous use of heparin. Bockus[17] suggested the use of this drug in portal thrombosis. Heparin is the anticoagulant of choice in portal vein thrombosis. It acts rapidly, is well tolerated over a wide range of dosage, its effects are easily reversed. It is not contraindicated in the face of hepatic dysfunction as is Dicumarol, and possibly it has a lytic effect on thrombus formation, not shared by Dicumarol.[31,32]

A case report illustrating the curative effects of heparin in acute thrombosis of the portal vein is presented.

Case Report

A 53 year old white man was first seen by us on July 30, 1953, complaining of abdominal pain of four days duration. Two weeks previously, mild epigastric distress had been present for a few hours, but had subsided without incident.

Generalized upper abdominal pain had developed suddenly on July 26, 1953, being more intense in the epigastrium. The distress was steady with cramping overtones, and radiated into the back. Nausea, anorexia, malaise, weakness, and temperature of 100° also appeared. No relief was obtained from soda, position, food, or enemas. Emesis occurred only once. Medical attention was not sought immediately because of the Christian Science faith of the patient's mother. There had been no previous dyspepsia or abdominal distress of any sort.

On admission, the patient appeared to be well developed and acutely ill. The face was flushed. The blood pressure was 170/90 mm. Hg. The temperature was 100.4°, the pulse 88 and the respirations 18 per minute. Physical examination was unremarkable except for moderate epigastric tenderness without masses or rigidity; the liver and spleen were not palpable. No stigmata of liver disease were evident. Typical postphlebitic changes were observed in the left lower extremity; moderate varicosities were present.

The patient gave a *past history* of thrombophlebitis involving the left lower extremity in 1918, and again in 1952. In April 1953 he developed intense headaches, lasting several weeks, and for which no cause had been found. A moderately heavy alcohol intake was admitted. He did not use tobacco.

Special Studies. The admission hemogram revealed 15 grams of hemoglobin with a hematocrit of 52 per cent. The sedimentation rate was 26 mm. in one hour (Westergren). There were 9,150 leukocytes per cu. mm., with 2 basophils, 2 eosinophils, 5 stab cells, 79 segmented neutrophils, 9 lymphocytes, and 3 monocytes per 100 cells. Other pertinent laboratory data are summarized in table 4.

A barium enema revealed a normal colon. Cholecystograms failed to visualize the gallbladder on two occasions. X-ray studies of the upper gastrointestinal tract were interpreted as disclosing a large hiatal hernia, antral gastritis, mild prolapse of the antral mucosa into the duodenal bulb, a wide duodenal loop, and segmentation and pooling of the barium in small bowel loops of greater than normal diameter (Fig. 1).

Course. The patient became progressively more ill. Frequent injections of Demerol were required to control his pain. His fever rose to 103°. Nausea and vomiting became marked; he was constipated. He became progressively more toxic and confused. The physical findings remained unchanged. The leukocyte count rose to 32,800 per cu. mm.

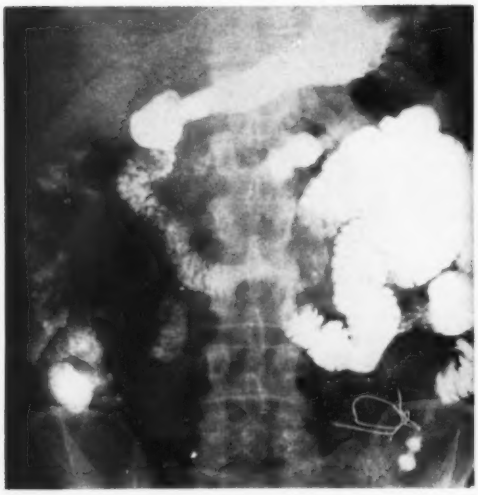
The diagnosis was not obvious. The patient presented a picture of a severe pathologic process of acute onset, producing pain, toxicity, fever, nausea, vomiting, constipation and confusion, associated with laboratory evidence of hepatic, pancreatic, cholecystic, and small intestinal dysfunction. It was felt by all of us that the exact nature of the disorder could be established only by laparotomy.

TABLE 4

BLOOD CHEMISTRY AND LIVER FUNCTION TESTS

	Pre-operatively	*Post-operatively 3 Weeks*	*Post-operatively 2 Years*
Cephalin flocculation	1+	2+	1+
Alkaline phosphatase	4.0		2.2
Thymol turbidity (units)	2.6		0.8
B.S.P. retention	18%		17%
Prothrombin time	20%	62% and 100%	100%
Prothrombin (After vitamin K)	100%		100%
Total proteins	6.83	5.4	6.8
Albumin	4.72	3.08	4.27
Globulin	2.56	2.3	2.5
Icterus index	6.9	7.7	
Serum bilirubin	0.5		
Amylase (units)	79 and 109		85
Glucose tolerance	Diabetic	Normal	Normal

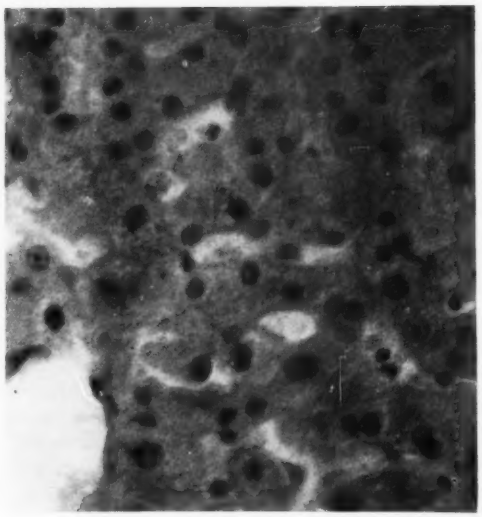
FIG. 1, A



He was explored by one of us (J.W.L.) on August 6. The gallbladder was collapsed. The liver appeared to be normal except that the color was much darker than the average. The portal vein was found to be thrombosed from the hilum of the liver to within 8 to 10 cm. of the wall of the small intestine in the superior mesenteric vein. The venous arcades of the small intestine were open but distended; the mesentery was discolored. The spleen was only slightly enlarged. There was no ascites. By palpation the splenic vein was thought to be thrombosed, but it was not visualized. The pancreas was moderately enlarged and very firm throughout; it was smooth and contained no masses. The stomach and duodenum were normal to appearance and palpation; there was a large hiatal

FIG. 1, B

FIG. 2, A

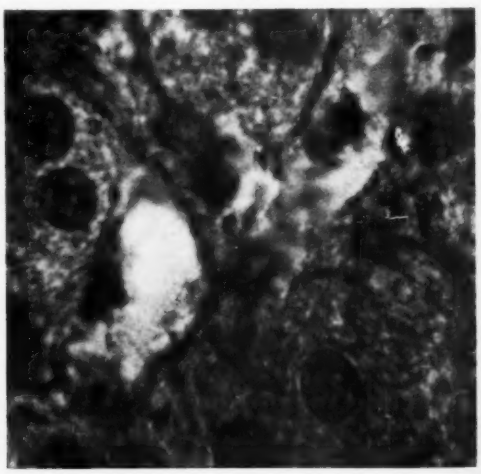


hernia. The coronary vein, epiploic veins, veins in the gastrosplenic ligament, and veins about the cardia of the stomach were distended and large. The small bowel appeared congested and slightly edematous, but was unquestionably viable. The pressure measured in a large epiploic vein was 40 cm. of saline. A liver biopsy was taken and the abdomen closed. The liver biopsy was later reported as being essentially normal except for mild fatty metamorphosis (Fig. 2).

Postoperatively he did poorly and had to be kept in the recovery room for three hours. His blood pressure rose to 260/160, and respiration was not satisfactory without an endotracheal tube.

By the next day his blood pressure had dropped to 100/70; the pulse was good and there were no signs of shock. On the second postoperative day he had ex-

FIG. 2, B



pelled flatus and had a soft stool. A liquid diet was begun. His abdomen was soft, flat and nontender. Heparin, 50 mg. intravenously every six hours was started. On the third postoperative day this was increased to 50 mg. every four hours subcutaneously. At this time his pulse varied from 90 to 110, and his blood pressure was 140/90. His temperature was normal. During the next four days his confusion continued, but otherwise he did well. He continued to have 2 to 3 soft stools daily. By the eighth postoperative day his confusion disappeared and he remained clear thereafter. He gradually improved for the remainder of his hospital stay. The heparin was tapered off and he was dismissed on September 4, the twenty-eighth postoperative day.

He got along well until September 26, 1953, when he developed a thrombophlebitis of the left long saphenous vein in the midthigh region. He was again hospitalized and given heparin. The phlebitic process subsided and he was dismissed on October 7. At this time his liver function tests were normal.

He was readmitted on December 7, 1953, January 2, January 21, and January 31, 1954, with thrombophlebitis of the right external jugular, right subclavian, and right brachial veins. Each time the process subsided promptly on heparin therapy, only to reoccur elsewhere. On the last admission he was put on Dicumarol instead of heparin and was dismissed from the hospital on maintenance doses of this drug. He had prothrombin time determinations regularly while in the city. While on a trip in March, 1954, he decided he was doing so well he did not need to bother with checking the prothrombin time. He promptly began to bleed from the genitourinary tract and rectum. He returned to Jackson and was given vitamin K-1. This promptly controlled the bleeding. All medication was discontinued at that time. He has not had an episode of phlebitis since this time, and has remained well except for a lumbar disk syndrome.

A follow-up examination was made in September, 1955. The patient felt well in every way, having no complaints of any sort. He had gained some 24 pounds since the pylethrombosis. His blood pressure was 150/86. The physical examination was entirely unremarkable. The hemogram and platelet count were normal. His other laboratory data are summarized in table 4. Infra-red photographs of his abdominal wall revealed a normal venous pattern. An ether rectum-lung circulation time was 26 seconds. Cholecystograms revealed a normal appearing and normally functioning gallbladder. No esophageal varices could be demonstrated radiographically (Fig. 3).

No valid explanation for the recurrent thrombosing episodes can be given, despite detailed and exhaustive metabolic and hematologic studies which were repeatedly carried out. These have not been summarized here, not being pertinent to our primary thesis. Nor is there any logical answer available for the sudden cessation of the cycle. We have rather reluctantly diagnosed this as an instance of idiopathic migratory thrombophlebitis.

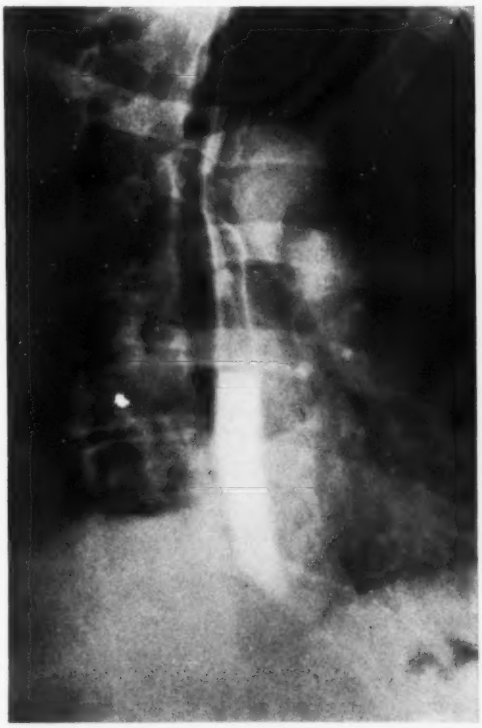
Discussion

We feel that this case exemplifies the life-saving effects of anticoagulant therapy in acute thrombosis of the portal vein of benign etiology, in this instance idiopathic migratory thrombophlebitis. It further illustrates that the clot itself does not kill, and that if the complications of the clot can be prevented, life can be saved. Heparin can accomplish this desired result.

Heparin is easily given and well tolerated when injected subcutaneously. We prefer this route to the intramuscular administration of depot type heparin because of flexibility of dosage, ease of control, and predictability of effectiveness. Determination of the Lee-White coagulation time two hours following any given dose accurately reflects its anticoagulant action. The dosage and frequency of administration may be adjusted to maintain the coagulation time at 18 to 24 minutes. Satisfactory results will be obtained in this range.

Although the preparation was not available at the time we originally saw this patient, we feel that serious consideration should be given to adjunctive therapy with intramuscularly administered trypsin (Parenzyme). Our re-

FIG. 3



sults with this agent in other types of thrombophlebitis convince us that it possesses genuine merit; it may prove to be of considerable value in the therapy of acute thrombosis of the portal vein as well.

The wide range of symptoms and the diversity of abnormal clinical findings in this case exemplify the extensive range of pathophysiologic derangement caused by this lesion. Hepatic, cholecystic, mesenteric, intestinal, and pancreatic dysfunction were evident. The degree of pancreatic involvement shown clinically as well as demonstrated at laparotomy is most intriguing and emphasizes the observations of earlier authors in this regard.[20,25,26]

The excellent functional recovery shown by this patient is most heartening. Although there is probably a moderately impaired blood flow to the liver (reflected in the bromsulphalein retention)[33] no other hepatic dysfunction can be demonstrated. The liver can again excrete Telepaque, hence the gallbladder is visualized radiographically. Pancreatic function has recovered; glucose tolerance is normal. The patient refuses esophagoscopy, percutaneous splenoportography, or hepatic venule catheterization. However, there is suggestive evidence that the portal pressure is not excessive in that varices cannot be demonstrated by x-ray, the spleen is not enlarged, and the ether rectum-lung circulation time is but slightly prolonged. No excessive collateral circulation can be demonstrated by infra-red photography of the abdomen. Manifestations of hypersplenism are not evident. The patient's feeling of health and general well-being is gratifying indeed.

The symptomatology of acute portal vein thrombosis may be obscure; the diagnosis may be most difficult. We recommend that once the condition is recognized, whether by clinical means or at laparotomy, the administration of heparin be immediately begun in conjunction with vigorous supportive measures.

By this means life may be prolonged or saved; a hopeless prognosis may become bright; salvage may be accomplished where otherwise none could be anticipated.

Summary and Conclusions

Acute thrombosis of the portal vein is relatively uncommon; it may be produced by a host of disease states, some benign, some potentially fatal in themselves. The pathophysiologic and clinical manifestations are briefly reviewed. The clot itself does not kill; death results from complications due to propagation of the clot. Anticoagulant therapy, preferably heparin, begun early in the course of the disease, offers a logical means of preventing these complications. A case is presented illustrating the successful results of heparin therapy in this lesion. The excellent functional state of the patient two years after recovery is noteworthy.

References

1. Morris, H.: Human Anatomy: A Complete Systemic Treatise, edited by J. P. Schaeffer, ed. 11, Philadelphia, Blakiston Co., 1953.
2. DeGaris, C. F., *in* Portis, S. A.: Diseases of the Digestive System, ed. 3, Philadelphia, Lea and Febiger, 1953.
3. Ingelfinger, F. J., *in* Sodeman, W. A.: Pathologic Physiology: Mechanisms of Disease, Philadelphia, W. B. Saunders Co., 1950.
4. Bradley, S. E., Ingelfinger, F. J., Bradley, C. P., and Curry, J. J.: The Estimation of Hepatic Blood Flow in Man, J. Clin. Invest. 24:890, 1945.
5. Bierman, H. R., Kelly, K. H., White, L. P., Coblentz, A., and Fisher, A.: Transhepatic Venous Catheterization and Venography, J.A.M.A. 158:1331, 1955.
6. Browne, D. C., and Welch, G. E.: Hepatic Catheterization and Upper Gastrointestinal Hemorrhage in Portal Hypertension, J.A.M.A. 158:106, 1955.
7. Welch, C. S.: Medical Progress: Portal Hypertension, New England J. Med. 243:598, 1950.
8. American College of Gastroenterology. Panel Discussion on Esophageal Varices, Am. J. Gastroenterol. 23:505, 1955.
9. Bierman, H. R., White, L. P., Kelly, K. H., and Steinbach, H. L.: Biochemical and Hematologic Characteristics of Blood From the Hepatic Portal Vein in Man, J. Appl. Physiol. 5:567, 1953.
10. Eck, N. V.: Ligature of the Portal Vein, Voyenno-med. j. 130:1, 1877.
11. Child, C. G., McClure, R. D., Jr., and Hays, D. M.: Studies on the Hepatic Circulation in the Macaca Mulatta Monkey and in Man, Surgical Forum, American College of Physicians, Postgraduate Medicine and Surgery, Philadelphia, W. B. Saunders Co., 1952.
12. Pick, L.: Quoted by Simonds.
13. Madden, J. L., and Lore, J. M., Jr.: Surgical Anatomy of the Portal System, Surgical Forum, American College of Surgeons, Postgraduate Medicine and Surgery, Philadelphia, W. B. Saunders Co., 1952.
14. Lissauer, L.: Quoted by Rolleston and McNee.
15. Webster, L. T.: Quoted by Lichtman.
16. Lichtman, S. S.: Diseases of the Liver, Gallbladder, and Bile Ducts, vol. II, Philadelphia, Lea and Febiger, 1953.
17. Bockus, H. L.: Gastroenterology, vol. 3, Philadelphia, W. B. Saunders Co., 1946.
18. Johnson, C. C., and Baggenstoss, A.: Mesenteric Vascular Occlusion. I. A Study of 99 Cases of Occlusion of Veins, Proc. Staff Meet. Mayo Clin. 24:628, 1949.
19. Kelsey, M. P., Robertson, H. E., and Giffin, H. Z.: Portal Obstruction in the Syndrome of Splenic Anemia, Proc. Staff Meet. Mayo Clin. 23:195, 1948.
20. Simonds, J. P.: Chronic Occlusion of the Portal Vein, Arch. Surg. 33:397, 1936.
21. Horder, T.: Quoted by Lichtman.
22. Child, C. G., and Callow, A. D.: The General Problem of Portal Hypertension, Bull. Tufts New England Med. Center 1:1, 1955.
23. Child, C. G. III: The Hepatic Circulation and Portal Hypertension, Philadelphia, W. B. Saunders Co., 1954.
24. Case Records Massachusetts General Hospital, New England J. Med. 230:231, 1944.
25. Frerichs, F. T.: Clinical Treatise of Diseases of the Liver (Translated by C. Murchison) New York, Wm. Wood and Co., vol. 3, 1879.
26. Rolleston, H., and McNee, J. W.: Diseases of the Liver, Gallbladder, and Bile Ducts, London, Macmillan and Co., Ltd., 1929.
27. McKee, F. W., Witt, W. G., Jr., Hyatt, B. E., and Whipple, G. H.: Circulation of Ascitic Fluid: Interchange of Plasma and Ascitic Fluid Protein as Studied by Means of C_{14} Labeled Lysine in Dogs with Constriction of the Vena Cava, J. Exper. Med. 91:115, 1950.
28. Case Records Massachusetts General Hospital, New England J. Med. 247:647, 1952.

29. Ross, J. R., and Kepkay, P. H.: Portal Vein Thrombosis: A Case Report, Lahey Clin. Bull. 8:85, 1953.
30. Luke, J. C.: Mesenteric Venous Thrombosis: Treatment With Heparin, Lancet 1:552, 1943.
31. Edwards, E. A.: Varieties of Thrombophlebitis and Their Management, Mod. Concepts Cardiovas. Dis. 21:154, 1952.
32. Allen, E. V., Barker, N. W., and Hines, E. A.: Peripheral Vascular Diseases, Philadelphia, W. B. Saunders Co., 1946.
33. Bollman, J. L., and Grindlay, J. H.: Hepatic Function Modified by Alteration of Hepatic Blood Flow, Gastroenterology 25:532, 1953.

Discussion (Abstract)

Dr. John R. Kelsey, Houston, Tex. We want to thank Dr. Kleckner for his effective presentation of postnecrotic cirrhosis and his comparison with that of portal cirrhosis. The difference between these groups is striking and his observations are in agreement with those of other authors. I would like to emphasize that the separation of these two groups is based on differences in the gross appearance of the livers rather than on a clinical differentiation. A patient with post-hepatitic type of cirrhosis usually has a nodular or a lobular liver, rarely a granular liver. While the liver of alcoholic cirrhosis most commonly is of granular appearance, it may be nodular, or occasionally lobular. Therefore, there is not an absolute correlation between the etiology of the cirrhosis and the morphologic appearance. I was interested in Dr. Kleckner's selection of cases. It appears that some of his cases were selected on a clinical rather than on a morphologic basis.

Dr. Baggenstoss believes that regenerating nodules are responsible for portal hypertension since they distort the normal architecture of the venous circulation. He believes that the smaller and more numerous the nodules, the greater the degree of venous obstruction. Thus, the granular forms of cirrhosis may be expected to produce the symptoms of portal hypertension most frequently. This fits in nicely with Dr. Kleckner's findings in the natural history of post-necrotic cirrhosis as compared with portal cirrhosis.

Dr. Kleckner has pointed out that the treatment of post-necrotic cirrhosis is limited because hepatic insufficiencies and bleeding tendencies contraindicate shunt procedures and that the prognosis of these patients is usually poor. Recently, a group from Boston has shown in animals that with the use of hypothermia, surgical procedures may be feasible in the presence of severe liver impairment. More work is being done in this field which offers a hopeful trend in our thinking.

During the past year, an interesting observation has been made concerning the cirrhosis seen with hemachromatosis. Some of these patients who have had repeated blood letting as treatment for their hemachromatosis have shown definite clinical improvement. There are a few instances in which liver biopsies were made before and after a protracted period of treatment. In these, the cirrhosis process appears to have resolved. This suggests the possibility that cirrhosis is not an irreparable progressive disease. Possibly when more is learned about cirrhosis there may be more hope for relief of these patients.

Dr. Richard D. Haines, Temple, Tex. It is a pleasure to make a few comments on the presentation of Dr. Welch and his associates as to the assessment of the occlusive catheterization pressures in the hepatic venule. I had the opportunity of reading and studying this paper several weeks ago, and am in total agreement with his data. Although the test is relatively complex in so far as the mechanics is concerned, it is the first time that a practical, nonsurgical method is available for determining, from a dynamic standpoint, the much needed information relative to changing portal pressures. I am inclined to believe that either this test or a modification of it will yield interesting data as it is applied to further cases. For instance, we assume many factors being involved in the production of ascites, which I am sure Dr. Caravati (South. M. J. 49:363, 1956) will discuss in detail. But perhaps in some, elevated portal pressures may be the predominating factor, and if no contraindication exists otherwise, surgery may offer some beneficial effect. Previously these individuals may not have been subjected to surgery. Personally, though, I suspect we may use this test in the future in an assessment of changing pressures in cirrhosis as the disease changes either for better or worse with treatment, and thus perhaps learn the highest tolerable total pressure before hypertensive and other factors have produced initial or fatal hematemeses. At the moment, I am inclined to suspect in acute varix bleeding, this test is somewhat inferior to the splenoportograms, which not only help to localize the site of the obstruction but give additional data relative to the caliber of the vessels in cases in which shunt procedures are anticipated.

I would like to ask Dr. Welch two or three questions:

1. In his experience, what is the difference in the ratio of the pressures between portal and hepatic venule catheterization in early and in very far advanced cirrhosis?

2. Have you correlated this particular test with the rectum-to-lung ether test which is a simple test and certainly can be used momentarily under almost any circumstance?

3. You did not mention any, but have you recorded any pressures in infectious hepatitis, in individuals with or without splenomegaly, and would you like to make any statement as to the cause of splenomegaly and its relationship to portal hypertension in such instances?

4. What would you advocate in an instance in which the hepatic pressure has again risen to high limits in which the individual has already had, say, splenectomy and splenorenal shunt procedure?

Dr. Welch. My answers to Dr. Haines' questions are as follow:

1. The series is too small to draw specific conclusions with regard to the ratio of the pressures in early and late cirrhosis. However, in this group the correlations were better in the more severe cirrhotics.

2. We have not correlated the occlusive hepatic venular catheterization test with the rectum-to-lung ether test.

3. No patients with active hepatitis have been studied in our group, however, Dr. Davis has had experience with portal pressure alterations employing direct needling of the portal capillaries through the abdominal wall.

4. This situation represents a dilemma. Assuming the indications for portal decompression are evident,

either portacaval shunt or hepatic arterial ligation should be considered. Transthoracic esophageal varix ligation would be a more temporary measure.

Dr. William Davis, Portsmouth, Va. I would like to discuss for just a moment Dr. Welch's very interesting presentation. We, too, (my colleagues in New Orleans and recently at the Naval Hospital), have been interested in the problem of the recording of portal pressures. There are at least three other methods by which a direct approach to the portal pressure might be obtained. The most well-known, of course, is Eddie Palmer's technic of puncture of esophageal varices. Another is one which Dr. Sheila Sherlock and our group have been working on independently, that is, the determination of the intrasplenic tissue pressure, which is a mirror of the portal pressure. The third is a direct puncture of a portal vein radicle within the hepatic substance. Pressures made by all of these methods do confirm Dr. Welch's observations.

One physiologic, or pathophysiologic point which might alter the hepatic venular mirror of the portal pressure is the fact that in some instances of cirrhosis, at least, there is a direct hepatic arteriovenous shunt. What effect this has in altering the relationship of the hepatic vein pressure to the general portal pressure I can only question, but it is something which should be considered.

We have been successful in a case or two in using pressure determinations by hepatic vein catheterization and intrasplenic pulp to localize or exclude splenic venous thromboses as causes for portal hypertension and esophageal varices as opposed to intrahepatic portal venous obstruction.

If I might, I should like to answer the question concerning portal pressure in hepatitis. Dr. Stanley Reichman and myself at the Naval Hospital have studied approximately 35 cases of acute infectious hepatitis with determination of intrasplenic pulp pressure. Early in the disease, there is an essentially normal portal pressure ranging up to 150 mm. of water referred to intra-auricular level; at the height of a relatively severe instance of acute infectious hepatitis, the pressure rises moderately to a maximum of approximately 260 to 280 mm. of water, but in every instance these pressures have returned to normal with resolution of the disease.

Dr. Long (Closing). The diagnosis of acute thrombosis of the portal vein is sometimes, of course, rather difficult, as was pointed out by Dr. Posey. Probably the only way that the diagnosis could have been made in this case, at that time, was by operation. Recently, a method of visualizing the portal system by injecting a dye into the spleen has been developed. We might have used it in this case, but at the time I had had no experience with it and, in fact, did not suspect portal thrombosis before operation.

This slide is of another case Dr. Posey and I have just recently seen, which presented what I would call subacute thrombosis of the portal vein, in that it had developed approximately 2 months before the patient was seen. This patient had Urokon injected into the spleen, as you can see; though it does not show up too well, I believe you can see the varices going up here. Here is a collateral and this one is a large one that does not show up too well. Here you will notice that the splenic vein does not show up at all; there are some more collaterals right here which can be seen much better on the original film. A liver biopsy was obtained previous to the splenoportography and the liver was perfectly normal. So we feel this is another case of portal thrombosis which has developed sequela to an acute portal vein thrombosis which occurred in July, 1955.

The diagnosis of acute thrombosis of the portal vein may be made in the future without surgery, by using hepatic venule pressures and splenoportography along with the clinical picture and other findings.

Another thing I want to point out is that the case reported by Dr. Posey has gone two years without any residual evidence of trouble except an 18 per cent dye retention. We cannot find any other evidence of portal hypertension at this time. I do not know how long it may be before he develops esophageal varices or some other sequelae. In fact, that is one of the questions we have had a long time, just what will happen to this man. So far, he has got along fine, and we hope he is going to be like the patient a surgeon sees, but possibly not the gastroenterologist, with iliofemoral thrombophlebitis of the leg. If these patients are treated properly, they will probably all get by and not have residual disease, but if the disease is not treated correctly and early, they will practically all end up with a post-phlebitic syndrome with which you are all familiar. So, we feel that by treating this patient early we may actually have prevented the development of what the other men have talked about today, namely, chronic portal hypertension.

One other thing has come up since that time, and that is whether one might use a trypsin preparation to supplement the anticoagulants. If I had to do this over, I would also add Parenzyme to the therapeutic regimen. In using it for peripheral thrombophlebitis, I do not know how this is going to turn out in a few years from now. I have been impressed with the fact that Parenzyme is actually of benefit in thrombosis of systemic veins and I believe it might be of some help in this type thing, too.

We feel the incidence of portal vein thrombosis, since we have seen two fairly recently, may be greater than we suspect. It may be that it accounts for a number of the instances of chronic portal hypertensions, and if it is recognized early and treated adequately, some or all of the late sequelae may be prevented.

The Causes and Significance of Delay in the Management of Adenocarcinoma of the Endometrium: A Review of 683 Proven Cases from the Philadelphia Pelvic Cancer Committee*

MILTON L. McCALL, M.D.,† *New Orleans, La.*

This paper dramatically appraises the price that is paid by a delay in the diagnosis of adenocarcinoma of the uterus. Furthermore, it points the finger at the shortcomings of the doctors in early diagnosis.

ADENOCARCINOMA OF THE ENDOMETRIUM is a lesion of increasing importance in the field of gynecology. There is mounting evidence that there exists an absolute increase in the incidence of this disease. Marshall[1] found that within a period of 10 years the number of endometrial cancers almost doubled. On our own service at Louisiana State University School of Medicine and Charity Hospital in New Orleans, the incidence has trebled since Weed[2] reported the unusually high ratio of one case of corpus cancer to sixteen of cervical cancer a few years ago.

Furthermore, with competent geriatric care, the span of life is lengthening for increasing numbers of the population which tends to augment the incidence of adenocarcinoma of the endometrium. While this neoplasm appears only once to every five cancers of the cervix in the younger age group, it becomes just as common as the latter by the age of 55 and more frequent by the seventies.

Unfortunately, even though this lesion is the most common, except for one, among pelvic malignancies, it is often relegated to a position of lesser importance in the consciousness of the physician. This may be because of the great emphasis placed on the problem of carcinoma of the cervix, or due to the intense interest fostered in many by the large and interesting variety of ovarian tumors which, however, are not as frequently seen. Cancer of the body of the uterus is usually a comparatively slow growing tumor, only gradually infiltrating through the myometrium and metastasizing to adjacent organs and lymph nodes relatively late. This accounts for an excellent prognosis in most cases. Paradoxically, these very facts seem to lull some of our profession into a false sense of security and loss of interest.

Among the factors which ultimately decide whether a patient with cancer will survive, these four are the most important: (1) the site of the lesion; (2) the degree of anaplasia present; (3) the extent of the disease; and (4) the type of therapy used.

While the site of the lesion and the degree of anaplasia are beyond our control, the extent of the disease present is basically dependent upon how early the diagnosis is made. This is the responsibility of both the patient and the physician.

Finally, prognosis is dependent upon whether or not proper treatment is instituted promptly. This, with rare exceptions, is the responsibility of the physician.

It is evident, then, that while there are some factors beyond control, there are, most fortunately, others which definitely place in *our* hands the power to influence the outcome of the cancer patient. The most important of these are *early diagnosis* and *early adequate therapy!*

Is adenocarcinoma of the endometrium with its favorable prognosis being diagnosed and treated as early and as well as it should be? There is evidence that cancers in other parts of the body are associated with delay

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in their management, and it has been suggested that a goodly number of the women who die each year in the United States of pelvic malignancy have not had the full benefit of early diagnosis and prompt adequate treatment.

Much of this information has come from the Philadelphia Pelvic Cancer Committee[3,4] which was founded in 1945 to study possible factors of delay in diagnosis and management of all types of pelvic malignancy in women. This group studies the patients as soon as a diagnosis of pelvic malignancy is made, at a time when the facts of each case are fresh in the minds of the patient and the doctor. The work of this Committee has been so significant and so outstandingly helpful to the community that all medical centers would do well to follow in its footsteps.

I am very much indebted to the chairman, Dr. John Howson and the entire committee for the opportunity to study the material from its files, which constitutes the basis of this report.

Six hundred eighty-three cases of adenocarcinoma of the endometrium were observed during the period just prior to 1945, through 1953. There are available 273 patients for five-year follow-up study, who were treated in 1945, 1946, 1947 and 1948. The records are not from hospital charts but are based on the information garnered from the patients themselves by representatives of the committee and the records of each physician handling the cases. (A great deal of the follow-up work was done by my nurse, Miss Patricia Pyles, to whom I am most indebted.)

Types of Delay

The categories used are patient delay, physician delay, and a combination of patient and physician delay where each has contributed. There is also the group with No Delay. The small number of cases of Institutional Delay, where the lack of hospital beds, for example, has caused the difficulty, have been disregarded.

TABLE 1

683 PATIENTS WITH ADENOCARCINOMA OF ENDOMETRIUM

	Per cent
No delay	29
Patient delay	49
Physician delay	34
Combined patient-physician delay	12

TABLE 2

AVERAGE LENGTH OF PHYSICIAN DELAY[2]

Cervix	7.4 months
Fundus	13.7 months
Ovary	9.6 months
Vulva	19.0 months

In this study delay is said to exist on the patient's part if more than one month elapsed between the onset of symptoms and securing of medical opinion. Delay is assumed to exist on the physician's part if more than one month elapsed between the first visit of the patient and the establishment of a diagnosis. The postponement of definitive treatment for more than one month following the making of a diagnosis is a further cause of delay.

Table 1 reveals the incidence of the various types of delay in this particular group of patients. There was no delay in 29 per cent whereas 49 per cent were associated with patient delay and 34 per cent with physician delay. In 12 per cent there was both patient and physician delay.

The average length of delay varies with the site of the lesion (Table 2).

While there has been some improvement in the length of delay in the diagnosis and management of endometrial cancer since the studies started in 1945, this has been slight and not continuous. The average physician delay has been around 14 months since 1948 (Fig. 1). Adenocarcinoma of the endometrium therefore has delay associated with its proper management for a more prolonged period than any other type of pelvic malignancy except cancer of the vulva.

FIG. 1

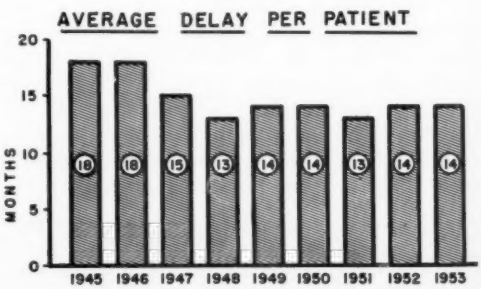


TABLE 3

FIRST SYMPTOMS

Postmenopausal bleeding	346		
Irregular or copious menses	242		
Watery discharge	34		
Leukorrhea	20		
Pain	20		
Miscellaneous	21		
Mass	2	Bladder Pressure	1
Fatigue	1	Incontinence	3
Pruritis	1	Hot flashes	1
Amenorrhea	1	No symptoms (6 with pyometra)	11

Symptoms

The symptoms which appeared first, although somewhat varied in a few patients, are quite straightforward (Table 3). It is evident, therefore, that the cause of delay is not due to vagueness of symptoms but rather to the fact that they are not interpreted as being possible significant signs of cancer.

Maliphant[5] found that 80 per cent of his cases were postmenopausal when they developed fundal malignancy, and Parsons[6] pointed out that 35 per cent of women with this disease had bleeding after the age of 51 years.

In our series the average age at the time of diagnosis was 59 years. Fifty-one per cent of these (346 cases) had postmenopausal bleeding and 35 per cent (242 cases) had irregular or copious menses at the time of the menopause or before. Thus 86 per cent had abnormal bleeding as the presenting symptom. Eight per cent had abnormal vaginal discharge other than bleeding and in most of these it was described as watery. In only 3 per cent was pain the symptom which prompted the patient to seek medical advice.

Causes of Delay

Patient delay was present in 49 per cent of cases, 37 per cent being entirely the fault of the patient, while in 12 per cent there was also a factor of physician delay. The causes and their frequency of patient delay are enumerated in table 4. In many cases a doctor was not visited even though definite symptoms were present. This was due either to the patient's ignorance that such signs were important or due to the fear that she had incurable cancer or some other fear concerning doctors or hospitals. Patient delay was also brought about by some who refused to follow the doctor's orders as to follow-up visits and diagnostic procedures, or refusal of part or all of the therapy recommended even after the diagnosis was made.

TABLE 4

CAUSES AND INCIDENCE OF TYPES OF PATIENT DELAY

	Per cent
Physician not visited (delayed examination)	
Due to ignorance	78
Due to fear	13
Physician visited (prompt examination)	
Therapy refused or delayed (poor cooperation)	9

Seventy-eight per cent of patient delay was apparently due to ignorance. The feeling was common that bleeding was not to be worried about during the postmenopausal period or that irregular bleeding was to be expected at the time of the menopause. Only 13 per cent admitted that they delayed because of fear of visiting a physician. Nine per cent went to a doctor within one month of the onset of symptoms but delayed in accepting medical advice along the lines of diagnosis or management. Very few refused all therapy for very long, but several had evident advance of their disease by the time they came back willing to undergo therapy.

Physician delay was present in 34 per cent of cases, 22 per cent being due to the doctor alone. Three main categories were evident here (Table 5). In many, no pelvic examination was done. This sad omission was carried on by the several doctors consulted, and over many months in some cases. Secondly, even though pelvic examination was carried out, the diagnosis was missed or the necessary procedures for the making of a correct diagnosis were omitted. Finally, there were some patients in whom a correct diagnosis was made after complete examination and study but where incomplete or erroneous therapy was carried out.

Forty-five per cent of physician delay was due to the fact that the doctor did not take the trouble to examine the patient even

TABLE 5

CAUSES AND INCIDENCE OF PHYSICIAN DELAY

	Per cent
A. Pelvic examination not done	45
B. Examination done	
1. Missed diagnosis 2. Insufficient study	40
C. Correct diagnosis, inadequate therapy	15

though she had definite suggestive gynecologic symptoms (Table 5). In 40 per cent the diagnosis was missed or necessary follow-up and diagnostic procedures were not done. Fifteen per cent were given inadequate or erroneous treatment.

Why were 45 per cent of symptomatic patients with adenocarcinoma of the endometrium not examined? As brought out in previous studies by the Committee[3] the most frequent reasons given have been: (1) trial of medication (usually hormones); (2) presence of bleeding; (3) typical signs of menopause; (4) patient "not ready;" and (5) first visit.

The fallacy of each of these reasons is obvious. In the second category, reasons for missing the diagnosis even though pelvic examination was done were several: (1) actual lack of knowledge on how to perform an adequate pelvic examination; (2) lack of facilities or equipment for good examination; (3) failure to advise curettement if uterus was not unduly enlarged; (4) assumption that obvious pathology such as senile vaginitis, cervical polyps, etc., were the cause of bleeding without performing curettage; (5) failure to do D & C before hysterectomy was carried out; and (6) failure to follow up patient carefully.

Inadequate treatment was the physician's fault in 15 per cent of cases. This was due mainly to: (1) ignorance of the correct therapy; (2) inability to carry out therapy; (3) refusal to consult; and (4) poor follow-up.

Salvage of Patients

Fifty-three per cent of 683 patients with adenocarcinoma of the endometrium lived for at least 5 years independent of stage of disease, therapy given or delay involved.

FIG. 2

SALVAGE ACCORDING TO STAGE OF DISEASE

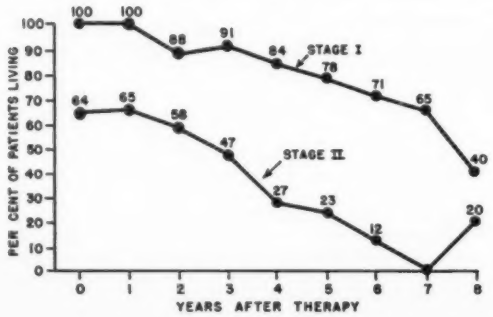


TABLE 6

FIVE YEAR SALVAGE RATE

	All	Stage I	Stage II
	%	%	%
No delay	63	79	14
Patient delay	47	79	14
Physician delay	51	61	29
Patient—Physician delay	53	75	8
Over All	53	75	16

For this study we have adopted the simplest method of classification by stages. Stage I includes all patients in whom there was no clinical sign of extension beyond the uterus. Stage II includes all patients with clinical signs of extension *beyond* the uterine body.

Figure 2 demonstrates the effect of stage alone on five-year salvage in spite of delay and type of therapy. The percentage of patients treated each year who were living on February 1, 1954 is shown. Zero represents the patients treated in 1953, one those treated in 1952, seven those treated in 1946, etc.

The effects of the types of delay on five year survival are shown in table 6. There was a 63 per cent salvage rate when no delay occurred, no matter what therapy was given or the stage of the disease. When the physician caused delay, the 5 year salvage was 51 per cent and when the patient was at fault it was reduced to 47 per cent. The average 5 year survival for all patients was 53 per cent, 75 per cent salvage for those with Stage I lesions and only 16 per cent for those with Stage II extension. Eighty-six per cent of the patients in Stage II were associated with some type of delay.

Patient delay reduced 5 year salvage to 46 per cent when ignorance was the main factor, but only to 60 per cent when fear was the motivating cause for procrastination (Table 7). The patients who refused or delayed the treatment advised by their physicians had a

TABLE 7

EFFECT OF TYPES OF PATIENT DELAY ON 5 YEAR SALVAGE

	Per cent
Delayed examination due to ignorance	46
Delayed examination due to fear	60
Therapy refused or delayed	44

TABLE 8

EFFECT OF TYPES OF PHYSICIAN DELAY ON 5 YEAR SALVAGE

	Per cent
No examination	52
Missed diagnosis	49
Inadequate therapy	44

30 per cent less chance of living for 5 years than those who cooperated promptly.

Physician delay also notably affected the 5 year salvage (Table 8). When pelvic examination was not done early and thereby the diagnosis missed, 52 per cent were living at the end of 5 years (17 per cent less than when no delay was present). When the diagnosis was missed in spite of pelvic examination, the delay was of greater significance and only 49 per cent lived 5 years. When inadequate therapy was given, whether further treatment was instituted at a later date or not, only 44 per cent lived 5 years; approximately two-thirds as many as in the "No Delay" group.

Comment

This study of 683 patients with adenocarcinoma of the endometrium reveals that advanced involvement is almost always associated with delay in diagnosis or management. When we consider that this type of malignancy possesses the brightest prospect for cure of all the major malignancies of the female genital tract, the failures due to the lack of prompt diagnosis and adequate therapy are all the more glaring and tragic.

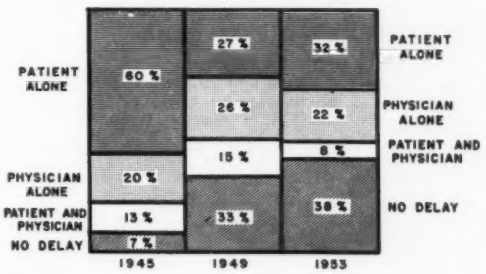
The specific types of therapeutic management have been disregarded in this evaluation of the various causes of delay and will be the subject of a further report.

When there was no delay in diagnosis and management, the 5 year survival was 63 per cent no matter what therapy was utilized. When there was either patient or physician delay, the salvage was markedly decreased.

The patient was a more frequent offender than the doctor. Seventy-eight per cent of patients put off seeing a physician because of ignorance of the importance of the symptoms they were experiencing. There was an increase of 27 per cent in the 5 year mortality rate in this group. Only 13 per cent stated that fear was the cause of delay and the 5 year survival was only 5 per cent less than in the "No Delay" group.

FIG. 3

DELAY IN DIAGNOSIS OF ADENOCARCINOMA OF THE ENDOMETRIUM



These figures suggest that there is a great need for continued and expanded education of the public in the importance of the early signs of uterine cancer. Furthermore, it would appear that the frightened patient is more apt to come for medical advice earlier than her less sophisticated sister and thereby reap the reward of a higher 5 year salvage. Such statistics can in no way condone the argument that attempts to educate the laity lead to cancer-phobia more devastating than the disease itself. The hypochondriacs who show such fear will usually focus their anxiety on some other fearful condition if it is not cancer. In the management of these few cases we agree with the sentiment that "the physician should not be as concerned about developing the reputation of alarmist as much as he should fear the responsibility for an avoidable death."

Almost 25 per cent of the delay in proper diagnosis and treatment of the patients in this study was directly due to dereliction on the part of the physician. The mortality became 20 per cent higher when the doctor failed. In spite of the many factors involved in physician delay, it is evident that "more mistakes were made by not looking than by not knowing," and that the most important aid the physician may have in the diagnosis of early cancer is "a well-developed sense of suspicion." There can be no question that there is a need for continued postgraduate gynecologic training.

Figure 3 shows the improvement which has been made from 1945 to 1953. The "No Delay" group increased from 7 to 38 per cent. This was due mainly to the fact that patient

delay was approximately halved during this period. It is discouraging to note that delay on the part of the physician has been almost stationary. The next great advance should come from the medical profession.

References

1. Marshall, S. B.: Endometrial Carcinoma: Study of 214 Cases from the Hartford Hospital, Connecticut M. J. 15:187, 1951.
2. Weed, J. C., and Chamblin, W. D.: Carcinoma of the Uterine Fundus, J. Arkansas M. Soc. 48:270, 1952.
3. Howson, J. Y., and Montgomery, T. L.: An Attack Upon the Delay Period in Diagnosis of Pelvic Cancer, Am. J. Obst. & Gynec. 57:1098, 1949.
4. Hahn, G. A.: Philadelphia Plan for Pelvic Cancer Control, J.A.M.A. 151:1166, 1953.
5. Maliphant, R. G.: The Treatment of Carcinoma of the Body of the Uterus, M. Press & Circular 211:313, 1944.
6. Parsons, L.: Carcinoma of the Endometrium, Rhode Island M. J. 32:668, 1949.

Discussion (Abstract)

Dr. Walter L. Thomas, Durham, N. C. I would like to recite briefly reports of two patients that illustrate the physician delay.

Number one is failure to examine. This 47 year old white para 3-0-3 came to us with the following story: She said that six weeks prior to her first visit to her local physician she began to have daily bleeding. She reported to him and he said that since she was bleeding he would not examine her that day. But he did notify her to return upon the cessation of bleeding. She was a very close friend of the doctor and she saw him during the next nine months on three social occasions and twice on the street. Each time he inquired as to whether she had checked bleeding, and each time she said, "I have not." So finally after nine months, she had a very profuse vaginal hemorrhage. She reported to him immediately and he examined her for the first time. He found her uterus about three times normal size and slightly irregular. He sent her to us with a preliminary diagnosis of fibromyomata uteri with profuse uterine hemorrhage. We found that she had adenocarcinoma of the endometrium with extension through the left myometrium to involve the upper left broad ligament, the left tube and ovary.

The next patient I wish to report will illustrate the second most common cause of physician delay, misdiagnosis. About 15 years ago, I was attending a session of the American Association of Obstetricians, Gynecologists and (then) Abdominal Surgeons in Hot Springs, Virginia.

Eleven months prior to the meeting a 60 year old woman had reported to an eminent gynecologist complaining of postmenopausal vaginal spotting and staining. He examined her and found that she had a mild atrophic vaginitis and an endocervical polyp about 0.5 cm. in diameter extruding from her os. He thought her uterus was atrophic. He estimated the size to be about 6 by 4 cm. He removed the polyp in his office and told the woman that he would send the microscopic report. He advised her to go home and quit worrying about the vaginal staining and spotting. The microscopic report of benign polyp was sent to the patient with another note of reassurance, informing her that she had nothing more to worry about.

Then the gynecologist stated, "That is where I failed miserably, because I neglected to tell that patient that if she had a recurrence of her bleeding after a week, to report back to me."

He then added that she continued to have spotting and staining daily. Finally, after six months, she had a very exsanguinating vaginal hemorrhage which promptly brought her back. On examination at this time, he found a 3 cm. ulcerative, nodular lesion in the lower posterior lateral wall of her vagina. A curettage of her uterus revealed adenocarcinoma of the endometrium. A biopsy of the vaginal lesion revealed metastatic adenocarcinoma.

To me, these two reports illustrate beautifully Dr. McCall's plea for us not to delay in diagnosis.

Is it not a sad commentary that here in the year 1955 we have a 14 months' delay in the diagnosis of adenocarcinoma of the endometrium, and a 19 months' delay in the diagnosis of an external carcinoma of the vulva? It seems almost incomprehensible.

Are you going to be guilty or am I going to be guilty within the next 12 months before another Association meeting of physician delay in the diagnosis of a fatal malignancy of the genital tract?

Dr. McCall is pleading with us that we have no physician delay.

Dr. Ralph E. Campbell, Madison, Wis. I was very much interested in Dr. Thomas' reciting the case of the very eminent gynecologist who told the patient that if she bled again, after her polyp was removed, she should have a diagnostic curettage. I still think he was in error. Do you? She should have had a diagnostic curettage at the time the polyp was removed.

The foregoing brings up the point that any woman who is having postmenopausal bleeding, no matter whether you find a polyp, senile vaginitis, a small fibroid uterus, a tumor of the ovary or no clinical findings, should have a diagnostic curettage.

Another interesting thing is this: One may do a diagnostic curettage and get nothing, but it is possible that one may have missed a small lesion with the curette, especially in the cornu of the uterus. In spite of this one may still have an inexplainable feeling that this patient has carcinoma and go ahead and take the uterus out and find the lesion which was missed by the curette.

The late Dr. Harris used to say in this type of case, "I would rather take the uterus out and find that she did not have carcinoma than fail to take it out and find that she had a small lesion up in the cornu of the uterus."

Public education is paramount. I do not know how we are going to do it, but we are trying and are failing in part. The American Cancer Society in conjunction with the Women's Federated Clubs went on a program to educate the women. They did not, however, get down to the level of ignorance and that is the problem. Every woman should know that postmenopausal bleeding is cancer until proven otherwise.

Dr. Joseph W. Kelso, Oklahoma City, Okla. I should like to stress one or two points. One is the reliance on a negative endometrial biopsy taken in the

office. I fear this gives a false sense of security. A positive biopsy is diagnostic, but a negative report should make it only more imperative that the patient be admitted to the hospital for a thorough curettage.

We have not seen this precipitous increase in endometrial carcinoma in our community. In fact, we have seen relatively few of such cases, which we believe can be explained by the fact that most of them are being operated on in the hospitals in their own communities and are not being referred to us as are the cases in which the malignancy involves the cervix.

My other point has nothing to do with detection but concerns treatment. The statistics as quoted do express the end result of some form of therapy. I have been for many years thoroughly convinced that radium has no place whatsoever in the treatment of endometrial malignancies. The numerous types of application of radium which we see in the literature convince one that the radiologists and gynecologists are not satisfied with the treatment and its results.

Two years ago, our department of gynecology started an investigation of operating on the patient without any intracavitary radiation, and x-ray therapy only if we find that the disease has extended through the serosal surface of the uterus or that evidence of pelvic or intrapelvic metastasis is demonstrable. Our recommendation is not a pelvic node dissection but a total hysterectomy, a bilateral salpingo-oophorectomy, and a liberal dissection of the cuff of the vagina.

Of course, all the statistics available today would overwhelm you if you were to consider any other treatment than that of radium followed by surgery, but that is because everyone has gained his statistical evidence from treating as it has been done before. However, I heard an eminent gynecologist from the northern section of the United States, who is a great proponent of preoperative intracavitary radium, state that he now questions whether the recognized standard type of treatment will stand the test of time.

With the few cases we see in our private services and in our medical school, more than our small group will be needed to gather adequate figures, to bring to you ten years from now, to disprove what I am stating or to prove that the statistics of today can be improved. I am convinced that we shall prove that the proper management of these patients is to operate upon them and not permit metastasis to occur during the six-week waiting period following the radium implantation.

Dr. McCall (Closing). I should like to thank the discussers, especially Dr. Thomas, for his vivid description of the significant cases which illustrate well several points which I have attempted to bring out in this presentation.

While this paper is not concerned with therapy, a subsequent presentation will take up this aspect of the problem of adenocarcinoma of the endometrium. I may say now, however, that the five year survival rate was more under the influence of whether or not there was delay in diagnosis and management than upon the type of therapy carried out.

Recently, there has been some controversy in lay journals concerning whether or not cancer propaganda is a good or a very bad thing. Some general surgeons apparently believe that cancer-phobia thus fostered is more serious than the disease itself. This is not true in the field of gynecology as proved again and again in many reports.

It is important, therefore, that we work together for the highest ideals in individual practice and in graduate training, so that in the near future, the pages in our textbooks which have to do with prognosis may be replaced by others upon which there will be figures far better than those of which we may boast today.

Dolitrone—A New Intravenous Anesthetic: A Preliminary Report*

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In the search for good analgesics, new drugs are brought out for study and trial. Such is the case with Dolitrone. The authors record their experiences with it.

SINCE THE DISCOVERY OF ANESTHESIA, nearly every depressant drug known has at one time or another been injected into patients' veins in an attempt to find an agent which would produce a satisfactory state of anesthesia. Although the advantages of intravenous anesthesia are well recognized and the search for suitable agents has been intense, only within the past two decades have the ultrashort acting barbiturates shown enough promise to have achieved general acceptance. Although these barbiturates represent a considerable advance over other drugs, they lack many desirable properties inherent in the inhalation anesthetic agents. The principal quality lacking is that of analgesic action.

Seeking an answer to this problem, the chemists of the Wm. S. Merrell Company set about to synthesize a compound which was not a barbiturate but, by virtue of its chemical architecture, should be a desirable intravenous anesthetic agent. The product of this effort was 5-ethyl-6-phenyl-*m*-thiazane-2,4 dione, called MRD-125 and later named Dolitrone. This agent was reported first in 1954 by Thompson, Smith and Werner.[1] The results of animal experiments by these workers indicated that Dolitrone was an intravenous anesthetic agent which possessed a higher margin of safety than thiopental, that there was little cumulative effect, that it did not seriously depress respiration, that laryngeal reflexes were depressed, and that muscular relaxation was good in doses which did not appreciably alter respiration. In addition, acute and chronic toxicity studies did not indicate that Dolitrone, in ordinary anesthetic doses, produced serious cardiac depression, renal, hepatic, or hematopoietic damage. Accordingly, a limited clinical trial of Dolitrone was begun.

The first detailed report of the use of Dolitrone in clinical anesthesiology was that of Lundy[2] of the Mayo Clinic. Although Lundy had mentioned this drug briefly in earlier publications,[3-5] his paper in 1954, at the meeting of the American Medical Association was the first to provide information on the clinical application of Dolitrone. At this time Lundy described the use of Dolitrone in 112 cases, 103 of which were dental extractions. Most of these patients received supplementation with nitrous oxide. In these papers he emphasized the striking degree of analgesia obtained, and held great hope for Dolitrone as an excellent analgesic agent. Lundy also mentioned the lack of respiratory and circulatory depression, the lack of relaxation of rectus muscles with absence of peristalsis, the ease of tracheal intubation, the absense of laryngospasm, and the apparent lack of peripheral vasodilation. He stated that in analgesia the electroencephalographic picture resembled that of thiopental, while in general anesthesia the pattern was that of cyclopropane. Comments were made also on the difficulty of getting the drug into solution, keeping it in solution, and its alkalinity (pH 11.5 to 12), but it was stated that thrombophlebitis was almost negligible.

In 1955, Kerr and Kahn[6] of New Orleans reported briefly on Dolitrone at a meeting

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of the Southern Society of Anesthesiologists. Although they felt that Dolitrone might prove to be a satisfactory intravenous anesthetic agent, they were very dissatisfied with the difficulties of solubility and the very high incidence of venous spasm attending injection of the earlier preparations available to them.

With this background, it was decided to explore further the potentialities of Dolitrone as an intravenous anesthetic agent and, if practicable, to use it as the sole agent for major surgical procedures. Through the kindness of Drs. Lewis and Allin of the Wm. S. Merrell Company, a small amount of the drug was made available to the Department of Anesthesiology of the University of North Carolina School of Medicine. To date, Dolitrone has been used in 68 cases, and this report is based on impressions gained from this very limited clinical trial, whose purpose was to determine whether or not Dolitrone possessed properties which might make it a useful general anesthetic agent.

Physical Properties and Problems of Solubility

Dolitrone is furnished as a lyophilized preparation of its sodium salt, a white crystalline powder which requires a slightly longer time to dissolve in water or saline than does thiopental. It is relatively insoluble in weak acids, and therefore dextrose solutions are unsatisfactory as a solvent. This fact may make the use of Dolitrone unsatisfactory in a continuous drip for it may require that undesirably large quantities of saline be given to a patient. It is our feeling that the intermittent injection of a 2.5 per cent solution in distilled water offers the most satisfactory method of administration. However, this solution may be given satisfactorily into a vein which is kept open by a drip of dextrose in water. It is probable that very soon preparations will be available which will be more soluble and permit the use of dextrose-water solutions, thereby facilitating the use of an intravenous drip method of administration. We have used concentrations as high as 0.6 per cent by drip, and feel that it will be necessary to use solutions of this strength if the drip method is to prove practicable.

After a solution of Dolitrone has stood at room temperature for a few hours, a clear crystalline precipitate is formed. This is said by the manufacturer to be the unchanged Dolitrone salt. The first preparations received would begin to crystallize after one to two hours. More recent lots of the drug, however, are easier to dissolve and remain in solution as long as four hours. It is recommended that stock preparations of the crystals be kept under refrigeration, and the solution be kept cold until ready for injection. Certainly, vast improvements have been made in the ease of solubility and stability of solutions of Dolitrone since the drug was produced originally, but further improvements are needed.

Venous Spasm and Phlebitis

In only one case has there been the problem noted by Kerr and Kahn,[6] i.e., venous spasm. In this case, three doses of 125 mg. each of a 2.5 per cent solution had been injected through the tubing of a 5 per cent dextrose in water drip in a vein in the right antecubital fossa. Further injection was impossible because of a marked venous spasm. This was accompanied by an urticarial wheal located approximately 4 cm. lateral to the cephalic vein at about the middle of the arm. Inhalation anesthesia was then instituted. No particular difficulties followed this venous spasm, and 48 hours later it was asymptomatic. A segment of venous thrombosis approximately 10 cm. long remained.

Venous thrombosis is not at all uncommon following the injection of thiopental, and whether or not Dolitrone is a worse offender in this respect remains to be seen.

Analgesic Action

The reports of Lundy had led us to believe that at the time consciousness was lost, a degree of analgesia adequate for skin preparation with water and pHisoHex, a pin-prick, or even for the introduction of towel clips would be present. This was not our experience. In every case in which Dolitrone was used as an anesthetic agent, it was necessary to give doses far in excess of the hypnotic dose before patients would tolerate preparation of the skin or the slightest painful stimulus. We have been most disappointed in the apparent analgesic properties of Dolitrone. To check these analgesic properties further, five normal humans were tested for threshold sensitivity of the dental pulp before and

after the intravenous administration of 0.5 mg. per Kg. of Dolitrone. This amount of drug produced mild drowsiness and dizziness but no change in the pulp sensitivity was noted. On another date, the same test was made on four of the original subjects using a dosage of 0.75 mg. per Kg. At this dose level a definite subjective sensation of drowsiness was produced, but in only one subject was there an increase in the sensitivity threshold of the dental pulp, and this was very slight.

Using Dolitrone as the sole agent for anesthesia, we have been quite impressed by the lack of evidence of analgesic action even when, by the usual signs, the patient was in surgical anesthesia.

Relationship Between Hypnotic and Anesthetic Doses

Patients receiving Dolitrone were premedicated with ordinary doses of pentobarbital (not exceeding 100 mg.), meperidine (not exceeding 100 mg.) and scopolamine or atropine. Using an intravenous drip (a practice which was abandoned) or the intermittent injection of 2.5 per cent solution, patients lost consciousness following the injection of as little as 100 mg. of Dolitrone, while one patient required 900 mg. before he ceased responding to the voice. At this point of minimal hypnosis, respiration was quiet and regular, and activity of the eyeball was present. At this level, however, the patients would move in response to a slightly painful stimulus, and it was not until several times the hypnotic dose had been given that the patients would tolerate the pain of a towel clip or surgical incision. At times skin preparation was permitted only after what we considered rather massive doses of Dolitrone. Once a dose had been given which would permit a surgical procedure to be started, it was found that added doses had to be given fairly frequently, but not as often as during induction, and intermittent injection had to be continued until near the end of the operation.

If the administration of nitrous oxide-oxygen by semiclosed inhalation at a flow of 2 liters of nitrous oxide and 1 liter of oxygen per minute is begun after hypnosis is established, it is our impression that induction is much smoother and less Dolitrone is needed for both the production and maintenance of surgical anesthesia. Consequently we have abandoned the use of Dolitrone as the sole analgesic agent and use it only to supplement nitrous oxide anesthesia.

In many cases supplementation with inhalation agents was begun after large doses of Dolitrone had failed to produce satisfactory anesthesia. In these cases it seemed that minimal concentrations of inhalation agents produced much smoother anesthesia and little additional intravenous agent was required. Whether or not Dolitrone possesses the same degree of cumulative effect as thiopental remains to be seen.

Pharyngeal and Tracheal Reflexes

One of the most striking observations in this small series of cases was the fact that oropharyngeal airways could be so easily tolerated by patients receiving Dolitrone. This was true even at light hypnotic doses and, although the patient might chew on the airway, cough, or swallow, laryngospasm was absent. Tolerance to an oropharyngeal airway was present after dosages far less than those required for the production of a satisfactory anesthetic state.

In many cases the larynx was exposed with ease and although the vocal cords were active, closure of the glottis was only momentary and respiration was relatively uninterrupted. When touched with an endotracheal tube, the cords adducted promptly but relaxed as soon as the stimulus was withdrawn. When the endotracheal tube was placed in the trachea, a series of three or four coughs resulted, but within a few seconds a smooth uninterrupted pattern of breathing followed. Bronchospasm and laryngospasm were not noticed to accompany instrumentation of the larynx or trachea, even when the plane of anesthesia was inadequate for surgery. This feature was most striking and in this respect Dolitrone certainly compares most favorably with other intravenous anesthetic agents.

Succinylcholine was employed to facilitate exposure in some cases, and in a few others topical anesthesia was used. It is our feeling at present that these adjuncts are desirable in selected instances, especially those in which exposure promises to be difficult for anatomic reasons or when coughing is highly undesir-

able, and we prefer to employ relaxants and/or topical anesthesia to large doses of Dolitrone.

One of us (D.C.G.) has obtained evidence that Dolitrone antagonizes histamine-induced bronchial constriction in dogs, but this impression requires further clarification.

Muscular Relaxation

In 3 cases Dolitrone was used as the sole agent for opening the peritoneal cavity. In many other cases the tone of abdominal musculature was estimated by palpation of the abdominal wall. It is our impression that tone of the abdominal wall is maintained, but that in most cases the abdominal muscles lacked the expiratory contraction, the "pushing," so often associated with light anesthesia. Packing off of intestines was easy and peristalsis was active. We do not feel that this absence of expiratory contraction of the abdominal wall is associated with the respiratory depression which accompanies deep anesthesia, nor do we have any evidence that Dolitrone possesses properties of a muscle relaxant.

Effects On Respiration

Unfortunately, apparatus for a detailed study of the effects of Dolitrone on respiration and ventilation was not employed in these cases. A few patients were studied using an ordinary basal metabolism spirometer. These studies coupled with clinical observation, suggest that at ordinary hypnotic dosages Dolitrone is not a respiratory depressant, but becomes a depressant when anesthetic concentrations are employed. Whether or not it is more or less depressing than thiopental or other anesthetic agents remains to be seen, and this aspect will be studied at a later date. The rate of respiration during Dolitrone anesthesia seems to be increased, and as anesthesia becomes lighter, the depth of breathing becomes deeper rather than the rate becoming faster.

We have been impressed by the finding that it is quite easy to take over control of the breathing of patients anesthetized with Dolitrone. Inflation of the lungs is very easy, and return of spontaneous respiration has been prompt. In this respect the lack of bronchial spasm is most gratifying.

It will be of interest to see whether or not Dolitrone will be useful in obstetrics. We have used the drug during the second stage of labor in two patients. In one, the mother had received no preliminary sedation and the baby was born apneic. Prompt resuscitation was effective, but the baby gave the impression of being drowsy. In the other case, the mother had been heavily sedated with a barbiturate and meperidine. Following the administration of Dolitrone and the delivery the baby cried promptly and the cry remained vigorous. In both patients the duration of anesthesia prior to delivery and dosages of Dolitrone were about the same.

Effects On Circulation

After the production of hypnosis with Dolitrone there occurred a slight fall in systolic blood pressure with little change in pulse rate. Whether or not this change is more or less severe than that produced by thiopental is speculative. During laryngoscopy there was noted a marked increase in pulse rate and blood pressure, with a return toward normal values following removal of the stimulus. During operations under Dolitrone alone, there was a consistent elevation of systolic and diastolic pressures with an increase in pulse rate. The tachycardia sometimes reached the alarming range of 140 to 160 per minute. Both the hypertension and tachycardia appeared to be related to surgical stimulation and disappeared when inhalation anesthesia was substituted or when the operation was terminated. These adverse effects on circulation did not seem to be corrected by deepening anesthesia with Dolitrone. Tachycardia and hypertension were much less noticeable in those cases supplemented with nitrous oxide from the start.

Miscellaneous Complications During Operation

Sweating was a fairly common complication of Dolitrone anesthesia, accompanied as a rule by hypertension and tachycardia. Whether or not this sweating was a sign of sympathetic stimulation is not known.

In two cases fine muscular fasciculations were noted. One instance occurred near the end of an operation and was controlled by the administration of 100 mg. of thiopental intravenously. In another case, muscular twitching appeared shortly after induction,

and after nitrous oxide supplementation was begun.

Discussion

Any evaluation of a new intravenous anesthetic agent must be based not only on a comparison of the new drug with a well-established agent such as thiopental, but on its properties relative to those of an "ideal" anesthetic agent. Although the present study has been directed toward an exploration of the field of usefulness of Dolitrone and obviously leaves much to be desired, it is felt that some impressions have been gained which will permit a few general statements regarding the usefulness of Dolitrone in the field of anesthesiology.

An ideal anesthetic agent should be stable, easy to prepare and administer, and provide a pleasant, quick induction. The induction of the hypnotic state with Dolitrone seems to be just as rapid and pleasant as with thiopental. The stability and solubility of Dolitrone still leaves much to be desired, although the manufacturers have made considerable progress in this field. The production of venous spasm and thrombosis is undesirable, but probably Dolitrone is no worse than thiopental in this respect.

One of the criticisms of the intravenous barbiturates is the lack of analgesic properties. In our experience the same is true of Dolitrone. It is our impression that this factor makes Dolitrone unsatisfactory as the sole agent for general anesthesia. On the other hand, when supplemented with an analgesic concentration of nitrous oxide, Dolitrone is a much more satisfactory agent than when used alone, but further study is necessary for an adequate comparison of thiopental-nitrous anesthesia with Dolitrone-nitrous oxide anesthesia.

It is necessary that a good anesthetic possess a wide margin of safety. This has been shown to be true of Dolitrone in the experimental animal. Our experience shows that patients will tolerate several times the hypnotic dose of Dolitrone without apparent harm; but also several times the hypnotic dose is required before satisfactory anesthesia is obtained.

Laryngospasm and bronchospasm are occasionally associated with thiopental anesthesia and when they occur they often reach serious proportions. It is our impression that if Dolitrone proves to have any advantage over thiopental it will be in the relative production of laryngospasm and bronchial spasm. The ease with which patients tolerate oropharyngeal airways and endotracheal catheters at light planes of hypnosis is most encouraging.

Minimal physiologic disturbances should be produced by anesthetic agents. No studies of alterations in hepatic, renal, or metabolic function were made on these patients, nor were many other studies made which will be necessary if Dolitrone is to come into greater use. We feel that respiration is not appreciably depressed during light surgical anesthesia with Dolitrone, but definite depresssion occurs in deeper planes. The most disturbing physiologic alteration is the hypertension and tachycardia which appeared in approximately one-half of the patients studied. No more detailed studies of cardiovascular function were made.

Recovery from good anesthesia should be rapid and free of nausea and vomiting. This is not true in the case of Dolitrone. Whether recovery from Dolitrone alone is more rapid than from thiopental is not known definitely, but recovery time when nitrous oxide supplementation is used is satisfactory. Vomiting in the recovery period occurred in 28 per cent of the cases.

Summary

1. The use of 5-ethyl-6-phenyl-*m*-thiazane-2,4 dione (Dolitrone) as an intravenous anesthetic agent in 68 cases is reported.

2. Dolitrone (as the sodium salt) is highly alkaline, insoluble in acids and relatively unstable in solution, precipitating in approximately four hours. The intermittent injection of a 2.5 per cent solution is the preferred method of administration.

3. Induction is rapid and pleasant.

4. There is a marked disproportion in doses required for hypnosis and the production of surgical anesthesia. Although previous reports emphasized the analgesic properties of Dolitrone, such properties were found to be lacking in these cases.

5. As a sole anesthetic agent, Dolitrone does not seem satisfactory. When supplement-

ed with nitrous oxide, a much better degree of anesthesia is obtained.

6. Tolerance of oropharyngeal airways is striking even in the hypnotic state. The relative absence of larynogospasm and bronchial spasm is most impressive. It is quite easy to secure control of the patient's respiration.

7. Besides lacking analgesic properties, the most disturbing feature of Dolitrone anesthesia is the appearance of tachycardia and hypertension. With nitrous oxide supplementation these manifestations are much less apparent.

8. The present study represents an effort to find a field of usefulness of Dolitrone and a satisfactory method for its administration. Subsequent studies will be undertaken to examine its pharmacologic activity in greater detail.

References

1. Thompson, C. R., Smith, J. K., and Werner, H. W.: Pharmacology of 5-ethyl-6-phenyl-*m*-thiazane-2, 4-dione, Fed. Proc. 13:411, 1954.
2. Lundy, J. S.: Development of Analgesia After a Century of Anesthesia, J.A.M.A. 157:1399, 1955.
3. Lundy, J. S.: 110 Years of Anesthesia, J.M.A. Georgia 43:195, 1954.
4. Lundy, J. S.: (Editorial) Will There Be An Era of Analgesia? Lancet 74:155, 1954.
5. Lundy, J. S.: Hope for an Age of Analgesia, J. Am. Assoc. Nurse Anesthetists 22:225, 1954.
6. Kerr, M., and Kahn, J. B.: Observations on Some Newer Drugs Used for Intravenous Anesthesia with Special Reference to Dolitrone. Paper presented at meeting of Southern Society of Anesthesiologists, April 16, 1955.

Discussion (Abstract)

Dr. Charles R. Allen, Galveston, Tex. I appreciate this opportunity to thank Dr. Davis for this report which is so timely and so needed. Many of us wish so strongly for an ideal analgesic drug that we too often grasp a new agent and say, "This is it," without first subjecting it to sufficient critical study.

As we summarize the findings of Dr. Davis it seems that the main advantage of Dolitrone is the obtunding of laryngeal and bronchial reflexes. Before we employ this agent for this one advantage we must carefully consider the disadvantages indicated by this report, namely:

1. Poor solubility (Present supplies are more readily dissolved than previous preparations but even these will precipitate within four hours)
2. Occasional vasospasm or thrombosis
3. Lack of analgesic properties
4. Respiratory depression in anesthetic concentrations
5. Tachycardia and hypertension (unless this agent is supplemented with nitrous oxide)
6. Sweating (Suggestive of autonomic or other physiologic imbalance).

Dr. John Adriani, New Orleans, La. One of the things I note when evaluating a drug is "Do the people who work with you use it voluntarily?" When the solution of Seconal became available and supplies we had given to us for investigational use ran out it appeared as though the department was paralyzed. The same thing happened while we were investigating xylocaine, allylnormorphine, and other drugs. With Dolitrone we usually have to get a bayonet and say "Now, let's use Dolitrone." As we take it into the operating room the surgeon looks at us and says "Oh, that stuff again. What are you mad at us for?" That is a good indication of how useful a drug is going to be.

Most of the information we have on Dolitrone is based on clinical impression. One of the difficulties we have had with it has been to get enough into a patient to keep him asleep long enough so that we could evaluate the substance. In the middle of an operation for instance the patient would all of a sudden cry out "Ouch that hurts." This is in agreement with the experience of Dr. Davis. The product that we have had has not been suitable for administration. Before anything is done with the drug it must be prepared so that the average "run-of-the-mill" person can administer it. If one has to go through a ritual every time he uses the drug no one is going to use it. That is one of the drawbacks with Dolitrone. Furthermore it takes some time to evaluate a drug pharmacologically. If one scans the literature, he will note that people are still investigating a drug such as morphine even though it was isolated in 1803. Here we have a drug that is a year and one-half old. Three or four workers have used it in the United States and everybody becomes enthusiastic. It has been claimed to be the answer to intravenous anesthesia. I doubt that Dolitrone is going to be the answer to our intravenous anesthetic problems but certainly the work should progress and the preparation which can be administered should be available before it is released to the profession at large.

Establishment of a Private Group Practice in Anesthesiology in a Small Community*

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The author provides the story of building a practice in anesthesiology in a moderately sized community.

PRESENTATIONS HAVE APPEARED IN THE LITERATURE in the last five or six years by Ausherman,[1] Webb and Leigh,[2] and Eather[3] concerning group practice of anesthesiology. All of these articles are concerned with the group practice of anesthesiology in large metropolitan areas. The purpose of this paper is to point out to anesthesiologists that the same kind of practice can be established in smaller communities, and to bring to your attention some of the complications which arise in the process of establishing this type of practice, as well as to point out the advantages both to the group of anesthesiologists and to the community.

The city of Alexandria, Louisiana, is a community of approximately 40,000 people. Across the Red River is the city of Pineville, having an additional 10,000 population. In this community are two private hospitals, one of 250 and one of 100 beds. Furthermore, there is a branch of the Charity Hospital of Louisiana located here with approximately 225 beds. In addition there are two mental institutions and a rather large Veterans Hospital. Thus, the physical facilities are available to support a group of anesthesiologists.

In this community there are approximately 75 physicians about half of whom are general practitioners, and the majority of whom practice in both the private institutions depending on the desire of their patients.

Let us turn then to the anesthesiologist. First of all it is necessary to have the desire, or at least the inclination to be happy living in a small community. Secondly, one must develop a philosophy about the size of the income which he will receive, since it of necessity will not be as large as the income of his acquaintances in larger cities. Once these two facts have been accepted by the anesthesiologist, the only real problem is that of a willingness to work long and frequently tedious hours, in order to give proper service to the patients, surgeons, and obstetricians.

I moved into this community in April, 1952, after having contacted many of the practicing physicians and having been assured by the majority of these that they were anxious for an anesthesiologist to move into the community. The administrators of the two private hospitals were consulted and both seemed anxious to have an anesthesiologist working in the community. However, it must be admitted that the hospital administrators were more interested in the anesthesiologist on a salary basis rather than in private practice. Nevertheless, staff applications were made and approved and I began working on April 1, 1952, with my personal equipment in both hospitals, and supplying all of my own drugs, trays, gases, and other supplies in order that I would not have to use equipment or supplies owned by the hospital. This was done in order to avoid double billing of the patient. Within a few months it was realized that in order to give proper service to the patients, surgeons and obstetricians it would be definitely advantageous to have at least one associate and probably more. I continued working alone until July, 1953, when I was joined by my first associate (R.H.M.). We worked on a partnership basis, and were joined in 1955 by two additional associates (W.R.A. and W.S.M.).

*Read before the Section on Anesthesiology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

When the third and fourth associates joined the group, the name of this partnership practice was changed to the Alexandria Anesthesia Service so that the firm name might remain the same even though the personnel might change. It was our opinion that the establishment of a known Anesthesia Service was more important than to retain a physician's name in the title of the group. The partnership works on a contract basis very similar in most respects to those described by Ausherman, Webb and Leigh, and Eather, there being only a few minor variations in the contract. One of these variations important to the group as a whole is the insurance program which we have carried. This is written into our contract in such a manner that in the event of death of one of the partners the claims of his dependents are settled by the payment of the insurance policy, which has been carried on his life, to the beneficiary. It is our opinion that this is a more satisfactory method of paying the beneficiary than the attempt to pay claims against unpaid receipts on the office books, because this could be detrimental to the remainder of the group.

Having discussed the evolution of this group, let us retrace our steps and point out some of the problems which arose in the course of carrying out this evolution. One of the first, and most upsetting, was the prophesy of several practicing physicians in the community that the practice of medicine and surgery had been satisfactory with the use of nurse anesthetists. Therefore, they predicted there would not be sufficient work for an anesthesiologist and he would undoubtedly be leaving town within six months. Obviously this prophesy was in error. An additional prophesy was that the cost of anesthesia by a medical anesthetist would make it prohibitive to patients, and that the cost would have to be double at least that which had been charged by the hospitals for anesthesia given by a nurse. Charges for anesthesia, prior to the arrival of the first anesthesiologist, were studied and the fees were considered to be quite adequate for him with a few exceptions. As a consequence it was not necessary to double the fees. As a matter of fact, there has been very little change, with few exceptions, in the fees which were being charged prior to his arrival. You can see that this was an obvious advantage to the anesthesiologist, but more important to the patient because he was getting better anesthesia and better care at little or no increase in cost. There has been a more stable fee schedule in our office than formerly, because our fees are based primarily on fee-for-service basis. Very little attention is paid to the factor of time which is given primary consideration by technicians. In the entire three and one-half years during which anesthesiology has now been practiced in this community, we know of only three complaints by patients in which our bills were considered too high, and, from a practical point of view, we know of more who have asked why their bills were not higher.

With the advent of the third and fourth partners and the formation of the Alexandria Anesthesia Service, one of the hospitals (St. Frances Cabrini) closed its nurse anesthesia service. Our group hired their two nurses and are now supplying all of the anesthesia service to this hospital. For the other private hospital we still schedule operations in our office at the request of the surgeon, obstetrician, or patient, and give anesthetics only in those cases which are scheduled in our office. The complete coverage at St. Frances Cabrini Hospital by our group has worked so satisfactorily, and the surgeons and obstetricians have been so pleased with this kind of coverage, that there has been a continuous undercurrent of pressure for us to give the same service at the other hospital. This has not been accomplished up to the present time, and it cannot be said when the final chapter in this evolution will take place, or what form it will take.

One of the extracurricular activities of our group consists of teaching the residents at the Huey P. Long Charity Hospital one morning a week on a rotating plan. These residents work on services under the supervision of the staffs of Tulane and Louisiana State University Medical Schools. This instruction has been a part of our program ever since the first one of us arrived in the community. We also are called occasionally to the Charity Hospital to give anesthetics in complicated cases, such as for intrathoracic procedures, occasional head injuries, problems of resuscitation, and other problems in which the anesthesiologist may be of paramount assistance. One of us (A.J.O.) is also on the consulting staff of the Veterans Administration Hospital although his services have not been utilized to any great extent by the institution, and

his visits to the Veterans Hospital have been few and far between.

Another thing which we occasionally have to do is go to one of the smaller neighboring towns with one of our surgeons who has been called in consultation to operate upon a patient in his home community. This practice is unsatisfactory to both surgeon and anesthesiologist, but we face the fact that some patients cannot be moved and that some in cases extenuating circumstances necessitate this type of service. Fortunately, for all concerned, this does not arise very often, but must be considered part of the service to the patient and surgeon when it does occur.

It seems to us that the evolution of this group of anesthesiologists has been of great benefit to the practice of medicine in this community. It is our belief that the entrance of any specialist into any community must, of necessity, improve the practice of medicine in that area. It is also our impression that this improved service to patients is of benefit to the entire community and not only to the medical profession. That, at least, is the impression we receive from some of our flattering friends in the Chamber of Commerce, many of whom did not know about medical anesthesiologists before 1952 and now wonder how the surgeons and obstetricians were willing to carry on without such help prior to that time. The division and sharing of responsibility by the anesthesiologist with the surgeon and/or obstetrician is something which the latter groups have learned to anticipate and utilize. This same division and sharing of responsibility is also something which the people of the community have come to realize, appreciate and value.

As stated before, the final chapter for this group has not as yet been written. Perhaps some day the final chapter of this growth will be accomplished, and we will then be able to write what is commonly known as the final report.

Summary

In conclusion, I have attempted to report the evolution of a small group of anesthesiologists in a small community. It is pointed out that this evolution must be slow and in proportion with the facilities of the community and its ability to support a group of anesthesiologists.

As a final word we would like to recommend to anesthesiologists that they investigate the possibilities of practicing this specialty in some of the smaller communities in the country, and not to feel that in order to be successful one must move into a large metropolitan area.

References

1. Ausherman, H. M.: Group Practice in Anesthesia, Anesthesiology 11:41, 1950.
2. Webb, Eric, and Leigh, Digby: The Private Group Practice of Anesthesiology, Anesth. & Analg. 32:199, 1953.
3. Eather, Kenneth F.: The Group Private Practice of Anesthesiology, Anesthesiology 15:689, 1954.

Discussion (Abstract)

Dr. Ray T. Parmley, Wichita, Kan. I enjoyed Dr. Ochsner's paper. He has put a lot of thought into its preparation. I would like to point out that before one goes out to practice one must prepare oneself. If you do not wish to join a group which I think is the easiest thing to do, you must prepare yourself to offer many community services.

During your residency, when your Chief has a program that brings out points other than how to drop ether, do not put up a mental block—learn about pain clinics, bronchoscopy and fluid therapy. Then when a surgeon has a problem he cannot handle he will call you. That is where you must build your foundation and not on the fact that you are an anesthesiologist and that you have your "Boards."

Other activities you will enjoy in a community where you introduce physician anesthesia are addresses to the groups such as the Boy Scouts or the local firemen regarding resuscitation.

I wish to thank the Program Chairman for the opportunity to discuss this paper.

Dr. Fred E. Woodson, Tulsa, Okla. I was very interested when Dr. Ochsner made the decision to leave New Orleans and to pioneer anesthetic practice in what is really not a small community but an average sized community, in which all the anesthesia had been done by nurses and the profits therefrom went to the hospital. That situation is common in many places in the South.

When I was Chairman of this group, my chairman's address was based on a survey I had made of all the hospitals in the South, and at that time there were about 400 full-time anesthetists in the South and 1,150 nurses, and that was not based on numbers from statistics; I even had the names and addresses of all of them in my survey.

But since that time, there have been many men who have had the courage to pioneer an anesthetic practice. The possibilities are even greater today, and hospital accreditation makes it a necessity to have, in a standard hospital of 100 beds or more, an anesthetic department which deals with, not only anesthesia but resuscitation, gas therapy, oxygen therapy, transfusions, water balance, and many of those things.

I say to you, if you have the courage to do as Dr. Ochsner did, there is opportunity in the South because there are many hospitals of fine quality which have

been built under the Hill-Burton bill in the South, and there are fields of adventure there.

If this Section has contributed one thing to anesthesia, it has been its encouragement because the papers that have been in the *Southern Medical Journal* have sold surgeons, who have had nurse-anesthetists in the past. Great men in surgery are now requiring men who have had formal training in anesthesia to come into their department. Some have a big enough surgical practice so they can almost engage a full-time physician trained anesthetist to do their work alone in their group. There is opportunity here and I want to encourage others who are now in training and who want to do that.

We have been fortunate in Tulsa in that in all the years that anesthesia has been in the hands of physicians, it has been on the private practice basis. That is where it ought to be, that is where it ought to stay. After you have practiced for a quarter of a century in a community, you have enough clientele, people for whom you have done a service and their families, that request your services, and it is a great pleasure to serve people in maybe three generations in anesthesia.

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Surgical Treatment of Diverticulitis of the Colon*

JAMES W. HENDRICK, M.D., *Tuscaloosa, Ala.*

The complications which may occur as the result of diverticulitis are considered, and the indications for surgical management are outlined.

DIVERTICULITIS OF THE COLON is observed in approximately 7 per cent of our population past 50 years of age. This disease, which is produced by irreversible structural changes in the colon, is of interest to the physician, surgeon, urologist, pathologist, gynecologist and radiologist. Case,[1] in 1915, demonstrated diverticula of the colon with roentgen-ray studies following administration of a barium meal. Carman[2] of the Mayo Clinic utilized roentgenographic studies with the barium enema to demonstrate multiple diverticula of the colon in 1923. In 1927, Spriggs and Marxer[3] found diverticulosis in 10 per cent of consecutive radiologic examinations of the colon using barium enema studies; they described a peridiverticular state of the colon as saw-toothed or spiked in appearance.

Until recently conservative medical management was advocated for the majority of patients suffering from diverticulitis;[4,5] it was generally taught that surgical treatment was not indicated until severe complications developed.

It is an accepted fact that the future of the patient with diverticulitis is quite unpredictable. Progress of the inflammatory changes may be slow or rapid without manifestation until perforation develops.[6] At operation it is not unusual to observe advanced inflammatory changes in the descending or sigmoid colon although the patient may have had only occasional severe symptoms.

Surgeons with extensive experience in gastrointestinal problems have discarded the ultraconservative attitude toward surgical therapy for diverticulitis with complications, and at the present time are utilizing properly timed primary one-stage resections with excellent results. Babcock,[7] in 1941, made an urgent plea for extending operative treatment of diverticulitis to an increased percentage of patients. At that time he wrote, "Diverticulitis of the sigmoid colon is one disease of an intra-abdominal organ characterized by a tendency to persist or relapse with perforation, peritonitis, abscess, fistula or intestinal obstruction for which leading surgeons still advocate medical measures and delayed palliative operations."

Jones[8] wisely commented, "I know of no abdominal ailment which calls for more individualization or taxes our surgical ingenuity more than diverticulitis and its complications."

Development of intestinal antiseptics and the advent of antibiotic therapy have removed the inherent risk of resection of any segment of the colon. Advancement in knowledge of fluid and blood requirements, anesthesia, and most important, the administration of surgical measures before serious complications develop, are decreasing morbidity and mortality rates.[9-14] Multiple stage operations formerly advocated in the treatment of this disease have become obsolete.

A comprehensive classification of diverticulosis and diverticulitis of the colon used by the author is as follows:

1. Diverticulosis
2. Diverticulitis with spasm and partial obstruction
3. Diverticulitis with complications of,
   - A. Perforation and abscess
   - B. Obstruction
   - C. Hemorrhage
   - D. Fistula and sinus formation
   - E. Complications simulating other disease (carcinoma or chronic ulcerative colitis)

*Read before the Section on Surgery, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

Incidence

We have observed diverticula present in 8 per cent of patients over 50 years of age during routine proctoscopic and roentgenologic examinations of the colon; symptoms of diverticulitis were present in approximately 20 per cent of this group. In a study[4,14] of diverticulitis and diverticulosis patients at the Massachusetts General Hospital over a three year period, these diseases were seldom observed below the age of 35 years. However, after that age there was a steady increase in frequency of the disease shown by the fact that diverticula were demonstrated in approximately 65 per cent of patients 75 years of age.

The disease is located in the lower descending and sigmoid colon in approximately 95 per cent of the cases. In this series of 40 patients who required surgical treatment, the average age was 55 years; 24 of these were women and 16 were men.

Etiology

The etiology of diverticula cannot be explained by any single factor. The accepted theory is that increased pressure in the colonic wall permits herniation of the mucosa at points of least resistance where the nutrient blood vessels and lymphatics pass through the muscular wall along the mesenteric border. Diverticula may occur on the mesenteric, antimesenteric, or lateral walls of the colon. This disease is more frequently observed in patients over 40 years of age when there is a loss of muscle tone and weakness occurs in the walls of the lower descending and sigmoid colon, in areas where the wall is thicker, its diameter is smaller, and the character of fecal contents is more solid.[15]

Pathology

The wall of a diverticulum of the colon, when complications are not present, consists of mucosa, submucosa and serosa. The size may vary from a few millimeters to 2 or 3 cm. in diameter, and if infection is present the diverticula may become much larger. The presence of uninflammed sacs are referred to as diverticulosis but when the mucous membrane is broken, and infection or inflammatory changes occur, the process is known as diverticulitis. The author has repeatedly observed in autopsy material that the neck of the diverticulum is smaller than the remainder of the sac; this in addition to lack of muscle in the wall of sac prevents expulsion of fecal material which constantly enters the sac. When infection develops in a diverticulum, edema, impairment of the blood supply and gangrene of the wall may result. The inflammatory reaction may be mild, moderate or severe and be confined to a single diverticulum or to a segment of the bowel wall.[12] If the inflammatory reaction is mild, there is resolution with no serious complications. However, repeated infections of this type produce fibrosis, thickening, and narrowing of the wall which contribute to partial obstruction and may simulate neoplastic disease. If the inflammatory reaction is severe, gangrene of the wall may occur and result in an acute or chronic perforation; the latter is more frequent.[15] If the perforation is acute and no inflammatory adhesions have formed around the inflammed diverticulum, a "blow-out" of the bowel wall may occur, resulting in a generalized peritonitis; two patients in this group had this complication.

The inflammatory process may involve longer segments of the bowel with development of peridiverticulitis with inflammatory adhesions to the small bowel, bladder, vagina, uterus or ureter. Perforation under such circumstances may result in abscess formation, fistula into the bladder, vagina, small bowel, ureter or rectum. Partial or complete obstruction may or may not develop. Frequently this advanced stage is the first definitive sign of the disease.

Diagnosis

Diverticulitis with Spasm. This disease occurs more frequently in middle aged or older corpulent individuals with sedentary habits who suffer from chronic constipation. These patients have recurrent episodes of cramping pain in the left lower abdomen; in some the pain becomes constant with alternating constipation and a number of loose stools daily. There may be abdominal distention, nausea, vomiting and elevation of temperature and pulse. Bladder irritability, accompanied by frequency and burning of urination is indicative of attachment of the inflammed diverticulum to the bladder.[16] Physical examination reveals tenderness and presence of a palpable

mass in the left lower abdomen, occasionally in the midline, with marked muscle spasm.

Diverticulitis with Complications. Patients suffering from recurring attacks of diverticulitis with spasm, who do not improve with competent medical management or who have severe symptoms from the beginning, may develop acute or chronic perforation with localized peritonitis and/or abscess. When these abscesses are drained a cutaneous fistula or sinus tract results.

In a review of 20 patients in this group having diverticulitis with severe complications, the symptoms and physical findings were more pronounced from the beginning (Table 1). The patients receiving medical treatment did not improve; on the contrary their pain became more severe; it was referred to the bladder, rectum and back. In three women the symptoms simulated an acute inflammatory infection in the left Fallopian tube. The temperature was elevated from 101 to 105 degrees; the leukocyte count varied from 13,000 to 25,000; there was marked abdominal muscle spasm with rebound tenderness. A mass was present in the lower abdomen in 14 patients; in 4 barium enema demonstrated barium outside the bowel lumen (Table 2).

Diverticulitis with Perforation. Two patients in this group of 20 had large perforations resulting in generalized peritonitis. One patient, a white woman 60 years of age, had no recognizable history of diverticulitis; her only complaint had been chronic constipation. She developed a sudden severe pain in the left lower abdomen accompanied by nausea, vomiting, elevation of temperature and pulse rate. After giving herself three or four enemas with poor results and with no relief of symptoms, her family physician was called and the patient was hospitalized. Her pain was so intense that two hypodermic injections of 100 mg. of Demerol did not give relief. When observed by me, 24 hours after the initial attack, there was evidence of a perforated viscus and the patient was in a state of shock. Blood transfusions and supportive measures were begun to relieve the shock state, and she was prepared for operation. When the abdomen was opened several hundred cubic centimeters of enema fluid and fecal material were found and a generalized peritonitis was present. The abdominal cavity was drained, and the patient was treated with antibiotics, blood transfusions, oxygen, and supportive measures but expired 48 hours later. Autopsy revealed a very large diverticulum of the lower sigmoid colon that had perforated; the bowel wall was thickened and narrowed over an area of 10 to 12 inches and contained numerous diverticula, demonstrating that chronic diverticulitis had been present over a period of time.

The second patient, a man 56 years of age, suffered from recurrent attacks of pain in the lower left abdomen of a cramping nature, accompanied by chills, elevation of temperature and alternating constipation and diarrhea. Following a self-administered saline laxative and several enemas the patient developed a sudden severe pain in the left lower abdomen. Following the same pattern as in the previous case, the pain became more intense and the patient was hospitalized. He was in a state of shock with evidence of a perforated viscus when seen by me. At operation the lower abdomen was found to be filled with enema fluid and general peritonitis was present. Antibiotic therapy and supportive measures were given but the patient died 72 hours later. Autopsy revealed perforation of two large

TABLE 1

SYMPTOMS OF TWENTY PATIENTS WITH DIVERTICULITIS WHO HAD ONE STAGE COLON RESECTION

1. Episodes of lower abdominal pain	20
2. Alternating attacks of constipation and diarrhea	13
3. Subacute or chronic diverticulitis with persistent partial obstruction	11
4. Bladder irritability	10
5. Recurrent hemorrhage	6
6. Attacks of nausea and/or vomiting	16
7. Recurrent attacks of diverticulitis with spasm	18
8. Recurrent attacks of diverticulitis with mass, left lower quadrant	14
9. Diverticulitis simulating carcinoma	6
10. Diverticulitis simulating appendicitis	1

TABLE 2

OPERATIONS ON 20 PATIENTS WITH DIVERTICULITIS BUT WITHOUT COMPLICATIONS

	Number of Patients	*Number of Deaths*
Resection of cecum, ascending colon, end-to-end ileocolostomy	1	0
Primary resection of sigmoid colon, end-to-end anastomosis, cecostomy	10	0
Primary resection of sigmoid colon, end-to-end anastomosis	6	0
Primary resection of descending and sigmoid colon, end-to-end anastomosis, cecostomy	3	0
Total	20	0

diverticula in the sigmoid colon with no inflammatory adhesions present. The bowel wall was thickened by a subacute inflammatory process with marked narrowing over an area of seven or eight inches and contained numerous smaller diverticula.

Of the 20 patients who had severe complications, 4 with perforations and abscess cavities were drained elsewhere before being referred to me for treatment. Ten patients were observed with subacute or chronic diverticulitis with perforations and abscess cavities that were drained; a transverse colostomy was also done in each case (Table 3).

Diverticulitis with Recurrent Hemorrhage. Traditionally it is assumed that rectal bleeding and bloody stools are pathognomonic of carcinoma or polyposis of the lower bowel and rare in diverticulosis or diverticulitis.[17,18] Gross blood or tarry stools were present in 10 and occult blood in 4 patients of this group. One patient had both carcinoma and diverticulitis. Two patients had massive hemorrhages which required immediate transfusions. One 64 year old woman was seen in subclinical shock due to blood loss of such degree that 18 pints of blood were given during a four day period. This patient had received medical treatment for three years for recurrent attacks of diverticulitis with spasm and partial obstruction; surgical treatment had been deferred due to a cardiac complication. After the patient's condition became stabilized following the hemorrhage and the colon prepared, 16 cm. of colon containing multiple diverticula were resected with a primary end-to-end anastomosis. The patient was discharged from the hospital on the ninth postoperative day with no further evidence of blood loss. (A similar but different case is shown in figure 1.)

TABLE 3

TWENTY PATIENTS WITH ACUTE, SUBACUTE OR CHRONIC DIVERTICULITIS WITH COMPLICATIONS

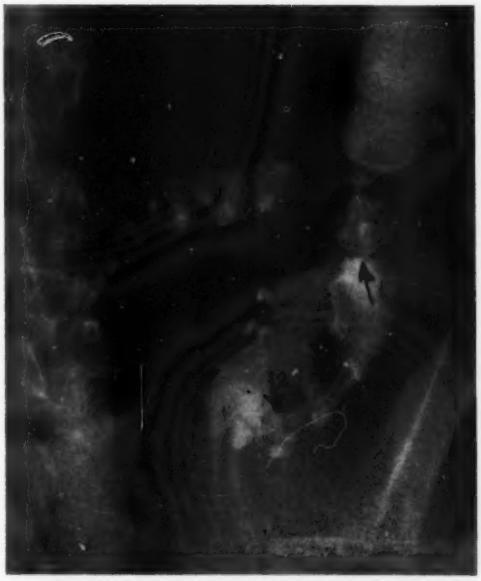
1.	Acute perforation with general peritonitis	2
2.	Acute diverticulitis with abscess formation	4
3.	Subacute or chronic diverticulitis with perforation and abscess	10
4.	Diverticulitis with bladder fistula	4
5.	Diverticulitis with cutaneous fistula	6
6.	Diverticulitis with fistula to vagina and/or small bowel	2
7.	Diverticulitis with multiple fistula	5
8.	Diverticulitis associated with carcinoma	1
9.	Diverticulitis with mass in left lower abdomen and obstruction	14

Patients with recurrent rectal bleeding should have a thorough lower bowel study to determine if hemorrhoids, polyps, diverticulitis or carcinoma are present. If no other disease is found it may be assumed that diverticulitis is the origin of the bleeding.

Diverticulitis with Obstruction. Anatomically the lower descending and sigmoid colon are narrower than the remainder of the colon. Consequently, when this segment is involved by recurrent attacks of diverticulitis there is infiltration of the bowel wall by inflammatory cells and fibrous connective tissue resulting in loss of elasticity, scarring, and narrowing of the lumen. Obstruction may also be produced by adhesions from a chronic perforation or pericolitis causing a segment of the colon to become adherent to the surrounding structures, i.e., small bowel, abdominal wall, uterus, ovary or Fallopian tube.

Twenty patients in this group had partial and 4 had complete obstruction. The sigmoid colon was involved in all except one patient in whom a loop of small bowel was adherent to a large inflamed diverticulum in the descending colon.

FIG. 1

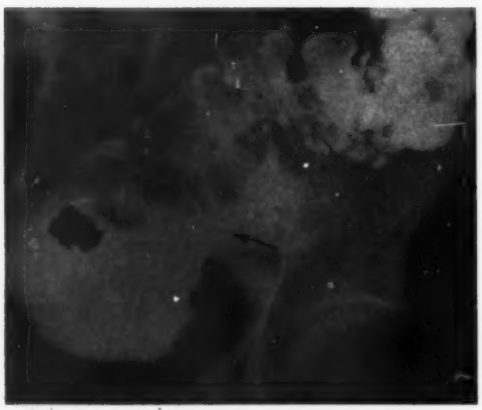


A white man, 58 years of age, had severe recurring attacks of diverticulitis requiring hospitalization three or four times each year. There was recurrent rectal bleeding. Roentgenogram shows polyp and multiple diverticuli of the sigmoid colon. Primary resection of the sigmoid colon with end-to-end anastomosis resulted in no further symptoms.

Diverticulitis with Fistula. No fistulas were present in the 20 patients who did not have severe complications. One of the most common sites for fistula is between the sigmoid colon and urinary bladder (Figs. 2 and 3); four patients had this complication,—three men and one woman. In two women the fistulas were between the sigmoid colon and vagina; one of these also had a fistula between the small bowel and sigmoid. Six patients had cutaneous fistulas. The 4 patients with fistulas between the colon and urinary bladder had symptoms referable to the urinary tract, i.e., frequency of urination, dysuria, pneumaturia, and recurrent attacks of chills and fever, in addition to bowel symptoms. Three of the 4 patients passed gas in the urine, 2 had barium pass into the bladder after roentgenologic examination of the colon by barium enema.

Differential Diagnosis. Frequently it is difficult to differentiate between chronic diverticulitis and carcinoma since both diseases may produce a tumor mass in the descending or sigmoid colon with partial or complete obstruction.[13,19] Gross and occult rectal bleeding may be present in both diseases; the patients are in the same age group. Hendrick and Adams[20] found, in a study of 337 cases of carcinoma of the colon and rectum, 114 or 33 per cent were located in the lower descending and sigmoid colon. In that series of patients 8 per cent had diverticulitis associated with carcinoma.

FIG. 2



A Mexican man, 61 years of age, had recurrent, severe attacks of diverticulitis over a period of four years. There was perforation of a diverticulum with abscess and bladder fistula. (Courtesy, Dr. Rodrigo Andalon, Coahuila, Mexico.)

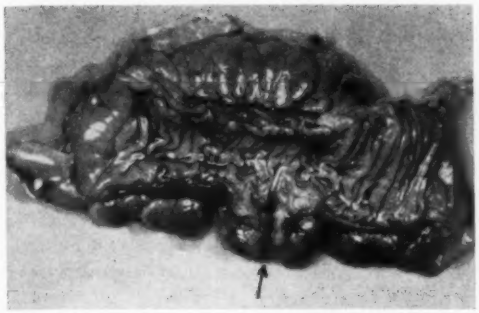
Diverticulitis produces a painful, inflammatory, immobile mass involving the outer wall of a longer segment of bowel than carcinoma and there is an associated leukocytosis and elevation of temperature. Carcinoma develops in the mucous membrane of the bowel wall and extends around the wall to produce an annular, painless lesion which is freely movable in its early stages. The progress of the patient with carcinoma of the colon is a gradual downhill course without remission in contrast to diverticulitis in which the patient is affected with recurring attacks.[21] Sigmoidoscopic and roentgenographic examinations are the most reliable methods of differentiating between these two diseases. The diverticula were located sufficiently low in eight patients in this group that the osteum could be observed through the sigmoidoscope.

Counseller[22] lists five signs by sigmoidoscopic examination which indicate diverticulitis: (1) limited mobility of a segment of bowel that is normally freely movable; (2) angulation of the upper part of the rectum due to inflammation; (3) reduced lumen and adherent mucosal folds; (4) sacculation of the sigmoid; and (5) visualization of the diverticula in the rectum.

Diverticulitis in women may present a diagnostic problem. An inflamed diverticulum may become attached to the left ovary, Fallopian tube or uterus to simulate an ovarian tumor or unilateral salpingitis.[22,23]

Diverticulosis and diverticulitis are not frequently encountered in the cecum or right colon but when present may simulate appendicitis, or carcinoma.[24,25] A 44 year old man in this group had recurring attacks of pain in the right lower quadrant referred to the right testicle, frequency of urination, nausea, and vomiting. On several occasions the pain was sufficient to require sedatives. The patient had an appendectomy elsewhere for chronic appendicitis, without relief of symptoms, 18 months previous to the time he was observed by me. There was a tender mass in the right lower quadrant which was first thought to be carcinoma of the cecum with perforation. Barium enema revealed a large diverticulum on the medial surface of the cecum that measured 6 by 8 cm. At operation, the mesentery of the terminal ileum, cecum, and part of the ascending colon was thickened and indurated; a diverticulum had per-

FIG. 3



Pathologic specimen of case shown in figure 2; perforation of the diverticulum with a fistulous tract extending into the bladder. Resection of involved area of the sigmoid with end-to-end anastomosis and closure of bladder fistula was done. Patient is symptom-free. (Courtesy, Dr. Rodrigo Andalon, Coahuila, Mexico.)

forated posteriorly. The bowel was densely adherent to the muscles of the posterior abdominal wall and right ureter. The terminal ileum, and ascending colon were resected with anastomosis of the ileum to the first portion of the transverse colon; the patient has been symptom free for four years.

Treatment

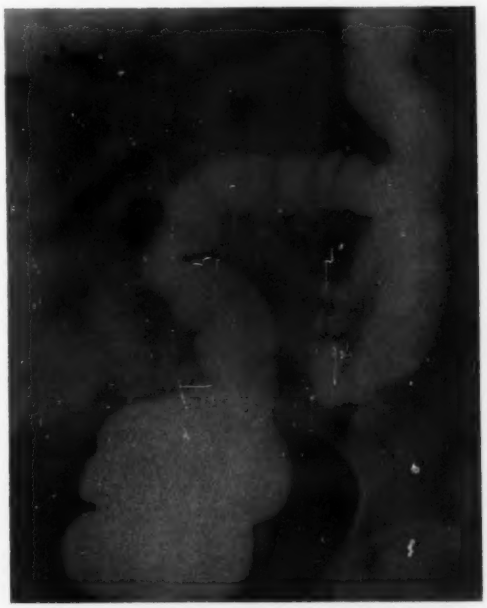
In general, diverticulitis of the colon is comparable to duodenal ulcer in that 80 per cent of patients in both cases can be managed medically. Surgery is reserved for the more severe recurring forms of each disease and for the complications. Sound medical judgment is essential in the management of patients with diverticulosis and diverticulitis. The patient should be appraised of his problem and cautioned to report evidence of complications. Medical management consists of a bland, nonconstipating diet, reduction of weight to normal if the patient is obese, and antispasmodic drugs. Many patients with acute diverticulitis with spasm can be satisfactorily treated medically by following a careful program. When the disease persists and evidence of complications develop, or when the patient is incapacitated every few months by recurring attacks of diverticulitis with spasm, surgical measures should be used. It is our policy to prepare these patients with antibiotics, especially in case of men who have urinary symptoms since we have observed that such patients frequently develop a bladder fistula.

In the past the accepted treatment for diverticulitis was medical until complications, i.e., perforations, abscess, fistula or obstruction, developed. When such complications are present the mortality and morbidity rates are increased and the patient is incapacitated for a longer period; this may be eliminated by the earlier use of surgical treatment.

Our group represents 40 patients with diverticulitis involving the colon who required surgical treatment. Twenty of these patients had unremitting, chronic diverticulitis without severe complications. Primary resection with end-to-end anastomosis was carried out with no mortality. The symptoms of these 20 patients who had a one-stage colon resection were episodes of abdominal pain, alternating attacks of constipation and diarrhea, bladder irritability, recurrent hemorrhage, partial intestinal obstruction, nausea and/or vomiting, and a mass in the left lower quadrant of the abdomen. In 6 patients, the disease simulated carcinoma and in one chronic appendicitis.

Of the 20 patients who had primary resections, 10 had resection of the sigmoid colon with an end-to-end anastomosis and cecostomy.

FIG. 4



A 62 year old female had recurring attacks of diverticulitis with marked spasm, partial obstruction over a period of five years. There was rectal bleeding. Resection of involved area of sigmoid colon with primary anastomosis was done. Early carcinoma was also present. She was symptom-free five years.

Six had primary resection of the sigmoid with end-to-end anastomosis. Three had involvement of the descending and sigmoid colon, making it necessary to resect the lower half of the descending colon along with the sigmoid colon with end-to-end anastomosis with cecostomy after the hepatic flexure had been mobilized. One patient had resection of the cecum and ascending colon with an end-to-end ileocolostomy.

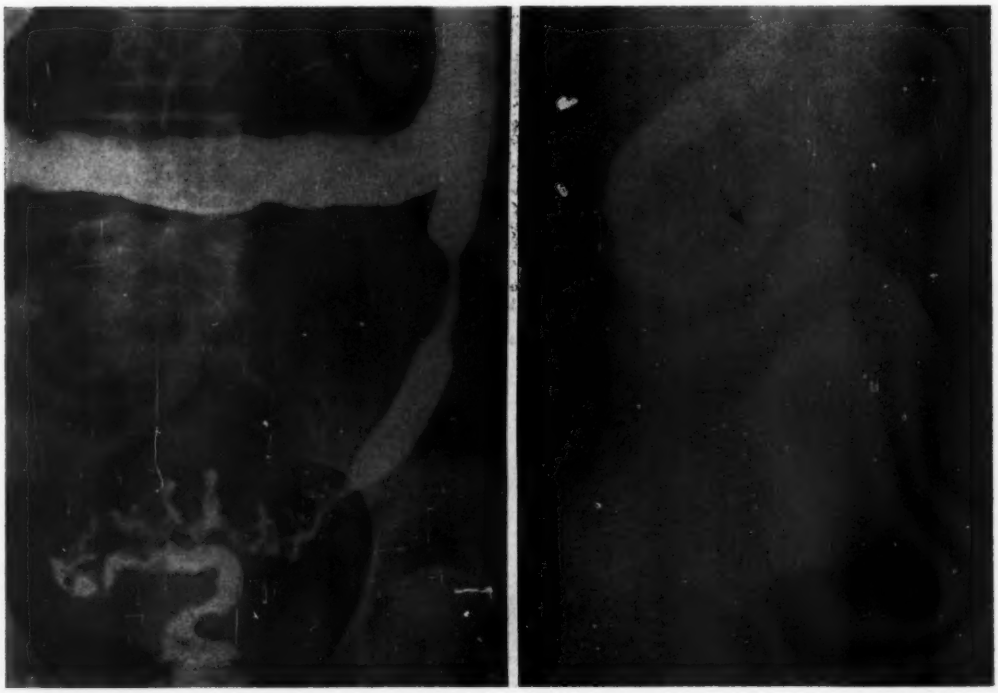
There were no serious complications in this group. One patient had to have nonabsorbable sutures removed in the upper area of the abdominal wound several months after the primary resection. This group of 20 patients had 20 surgical procedures with an average hospital residence of nine days.

Treatment of Diverticulitis with Complications. The other 20 patients of the 40 had diverticulitis with severe complications requiring multiple stage operations. The treatment of acute, subacute, and chronic diverticulitis with perforation, abscess formation, partial or complete (Fig. 4) intestinal obstruction and/or fistula presents very serious surgical problems.

Acute, subacute or chronic perforations into the peritoneal cavity with evidence of localization of an abscess warrants exploration and drainage; care must be used not to break down the walls of the abscess cavity. A transverse colostomy is established to prevent further contamination of the peritoneal cavity, to permit the diseased bowel wall to rest, and to aid in an earlier resection of the involved loop of colon with closure of sinuses or fistulas when present. The patient is treated with Wangensteen suction, adequate fluids, including blood transfusions, and antibiotic therapy.

Formerly when a transverse colostomy was performed following drainage of a localized abscess with or without fistula, it was not infrequent that the patient was either forced to keep the colostomy or, if it was closed after a period of several months or a year, to have a recurrence of the disease.[5,13] Consequently,

FIG. 5



A white woman, 68 years of age, had recurring attacks of diverticulitis for a period of ten years. There was chronic perforation with abscess and fistulous tract extending into the bladder. Resection of involved segment of colon with end-to-end anastomosis and closure of bladder fistula were done. Patient is symptom-free.

this method of management has been discontinued.

At the present time patients who have had a transverse colostomy following drainage of an abscess cavity, with or without fistulas, are prepared with antibiotic therapy as soon as feasible, usually eight to ten weeks thereafter, to permit the inflammatory reaction to subside in the (Fig. 5) involved area of bowel. Following this preparation the diseased segment of bowel is resected with a primary end-to-end anastomosis; after a period of two or three weeks the transverse colostomy is closed.

Fourteen patients with diverticulitis with complications in this group had acute, subacute or chronic perforations with abscess formation. Four had bladder fistulas; 2 had fistulas extending from the sigmoid colon to the vagina and/or small bowel. It was necessary to repair the bladder, vaginal or small bowel fistulas in 8 patients in this group. Six patients had cutaneous sinuses resulting from drainage of an abscess cavity; 4 patients with perforations and abscess cavities had the abscesses drained elsewhere.

Six patients who had a transverse colostomy for either obstruction with acute or subacute diverticulitis, later had resection of the sigmoid with end-to-end anastomosis. Six other patients had transverse colostomy and an exteriorization resection with closure of the colostomy after continuity of the bowel had been re-established. These cases were operated on before the advent of antibiotic therapy and exteriorization resections were safer at that time.

In contrast to the previous 20 cases without severe complications, these 20 patients with severe complications required 48 surgical procedures to eradicate their disease (Table 4). The average hospital residence was 42 days and there were two operative deaths. If the diagnosis had been established earlier and definitive therapy had been used before severe complications developed, the mortality and morbidity rates would have been substantially reduced in this latter group of 20 patients.

Indications for Operation. Operation is indicated in: (1) patients whose symptoms do not subside under medical management after a reasonable length of time; (2) patients who have recurring incapacitating attacks of diverticulitis while on a good medical program; (3) patients with diverticulitis who develop urinary symptoms; (4) patients demonstrating persisting deformity of the descending and sigmoid colon by roentgenographic examination; (5) patients with diverticulitis that cannot be differentiated from cancer; (6) patients with diverticulitis who have recurrent rectal bleeding; (7) patients with diverticulitis under 50 years of age; (8) patients with cytologic smears from rectal washings that are positive for cancer; and (9) patients with acute or chronic diverticulitis with perforation.

TABLE 4

FORTY-EIGHT OPERATIONS DONE ON 20 PATIENTS WITH DIVERTICULITIS AND COMPLICATIONS

Surgical Procedures	*Number of Patients*	*Number of Deaths*
Transverse colostomy, drainage of abscess	5	1
Drainage of abscess elsewhere	4	0
Transverse colostomy, later resection of sigmoid colon end-to-end anastomosis	6	0
Transverse colostomy, later exteriorization, resection	6	0
Resection of sigmoid, end-to-end anastomosis, cecostomy following drainage of abscess elsewhere	4	0
Resection of descending and sigmoid colon, following drainage of abscess, cecostomy	2	0
Exploration of lower abdomen, drainage	1	1
Closure of colostomy following resections	12	0
Repair of bladder, vaginal and small bowel fistulas	8	0
Total	48	2

Summary

A study has been made of 40 patients with diverticulitis of the colon of sufficient degree to require surgical measures to eradicate the disease. Twenty patients were treated before serious complications developed, i.e., perforation, abscess formation, obstruction, or fistula. In this group, the 20 patients had 20 operations which consisted of primary resection of the involved segment of colon with end-to-end anastomosis. The average postoperative hospital residence was 9 days.

Twenty other patients with severe complications required 48 operative procedures. There were two deaths which occurred in patients with massive acute perforations resulting in generalized peritonitis. The average postoperative hospital residence of this latter group was 42 days.

References

1. Case, J. T.: Roentgenologic Demonstration of Multiple Diverticula of the Colon, Am. J. Roentgenol. 2:654, 1915.

2. Carman, R. D.: The Roentgenologic Findings of Three Cases of Diverticulitis of the Large Bowel, Ann. Surg. 61:343, 1915.
3. Spriggs, E. I., and Marxer, O. A.: Multiple Diverticula of the Colon, Lancet 1:1067, 1927.
4. Albright, H. L., and Leonard, Field C.: Management of Diverticulitis Coli, Am. J. Surg. 82:674, 1951.
5. Pemberton, J. deJ., Black, B. M., and Maine, C. R.: Progress in the Surgical Management of Diverticulitis of the Sigmoid Colon, Surg. Gynec. & Obst. 85:523, 1947.
6. Lewis, Frederick I.: Editorial. Diverticulitis of the Colon, Ann. Surg. 130:983, 1949.
7. Babcock, W. W.: Diverticulitis, Rev. Gastroenterol. 8:77, 1941.
8. Jones, T. E.: Inflammatory Lesions of the Colon, Surgical Aspect, J.A.M.A. 126:1013, 1944.
9. Donald, J. M.: The Surgical Management of Diverticulitis of the Colon, Ann. Surg. 133:708, 1951.
10. Judd, Edward S., and Mears, Thomas W.: Diverticulitis, A.M.A. Arch. Surg. 70:818, 1955.
11. Moore, Robert M., and Kirksey, O. T., Jr.: One-Stage Resection in Selected Cases of Sigmoid Diverticulitis, Ann. Surg. 139:826, 1954.
12. Morton, John J., Jr.: Diverticulitis of the Colon, Ann. Surg. 124:725, 1946.
13. Smithwick, R. H.: Experiences with the Surgical Management of Diverticulitis of the Sigmoid, Ann. Surg. 115:969, 1942.
14. Welch, Claude E., Allen, Arthur W., and Donaldson, Gordon A.: An Appraisal of Resection of the Colon for Diverticulitis of the Sigmoid, Ann. Surg. 138:332, 1953.
15. McDonald, Dean: Sigmoidal Diverticulitis, Some Brief Clinical Notes, Am. Pract. & Digest Treat. 1:46, 1950.
16. Smith, Daugh W.: The Surgical Management of Diverticulitis of the Colon, Am. Surgeon 18:985, 1952.
17. Bell, H. Glenn: Bleeding in Recurrent Low Grade Diverticulitis of the Sigmoid, South. M. J. 46:453, 1953.
18. Noer, Rudolf J.: Hemorrhage as a Complication of Diverticulitis, Ann. Surg. 141:674, 1955.
19. Morton, John J.: Diverticulitis and Carcinoma of the Sigmoid, Surgery 32:765, 1952.
20. Hendrick, James W., and Adams, Thurston R.: Factors Influencing Operability of 337 Carcinomas of the Colon and Rectum, Texas J. Med. 43:641, 1948.
21. Neal, J. Walter, Jr.: Diverticulitis of the Colon and Its Surgical Management, Surgery 30:606, 1951.
22. Counseller, V. S.: Diverticulitis: Symptoms, Complications and Management, Particularly in the Female, Am. J. Obst. & Gynec. 55:653, 1948.
23. Johnston, M. Harlan, and Stubbs, George M.: Sigmoidouterine Fistula Complicating Diverticulitis, Ann. Surg. 141:704, 1955.
24. Unger, Harold M.: Solitary Diverticulitis of the Cecum, Am. J. Surg. 85:780, 1953.
25. Vaughn, Arkell M., and Narsete, Eugene M.: Diverticulitis of the Ascending Colon, A.M.A. Arch. Surg. 66:330, 1953.

Clinical Significance of Alterations in Gamma Globulin Levels*

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This reviews the knowledge of the recently proven and significant clinical state of deficiency in gamma globulins. The recognition of associated lack of immune response has been a most important event in the advance of medical knowledge.

DESPITE THE RECOGNITION OF RELATIONSHIPS between gamma globulin and generalized immune mechanisms, much still remains unknown about many of these problems. Certainly the role of gamma globulin in tissue immunity has not been clearly elucidated. Furthermore, it is quite likely that there are qualitative as well as quantitative differences in gamma globulin. Investigations in this field have led to the recognition of certain clinical entities. In recent years there have been numerous reports of alterations in the gamma globulin fraction with resultant profound effects upon antigen-antibody relationships. It is the purpose of this paper to catalogue these alterations.

Methods of Determining Gamma Globulin Levels

The separation and identification of the various protein components of serum may be accomplished in several ways: chemical salt fractionation, immunochemical technics, or electrophoresis (migration of colloidal particles under influence of an electric field). Precipitation of globulin fractions in different salt concentrations can be accomplished in the same manner that albumin is separated from the entire globulin fraction in routine determinations of serum proteins. However, this precipitation technic is influenced by so many physical factors that a reasonable degree of accuracy with this method cannot be expected under ordinary conditions.

Immunochemical procedures are invaluable for detection of trace amounts of protein, but methods are so technical they must still be regarded as research tools. However, recently Gitlin and Janeway[1] have described a simple screening method for the determination of gamma globulin utilizing the diffusion technic of Oudin.[2] Horse antisera against human gamma globulin is incorporated into a gel. The serum to be tested is placed over the gel and the results quantitated by measuring how far the band of precipitation has diffused into the interface after a given time at controlled temperature. However, until horse antisera which have been suitably adsorbed from other antibodies are made generally available, this method will not be widely used.

Electrophoresis now plays a significant role in certain aspects of medicine.[3,4] Classical electrophoresis-convection with the Tiselius apparatus while certainly accurate for quantitatively separating serum components, is so expensive and so complicated in determination that it cannot reasonably be made generally available. However, filter paper electrophoresis is simple and has been found practical as a screening procedure for measuring gross variations in gamma globulin levels.[5] Therefore, this method, as performed in our office, will be described in some detail.

The total equipment required can be procured for an expenditure of less than fifty dollars (Fig. 1):

1) Two shallow beakers or plastic dishes, each of about 200 ml. capacity.

2) Two pieces of plate glass measuring approximately 4 by 12 inches.

3) A small quantity of glass wool.

4) Whatman # 1 filter paper (available in ½ and 1 inch strips at most laboratory supply houses).

5) A 0.1 molar barbital-buffer solution with pH of 8.6. (Made by dissolving 20.62 Gm. of sodium barbituric acid and 2.49 Gm. barbituric acid in 1 liter of distilled water. This solution is a stock buffer solution and should be kept refrigerated. It is diluted with an equal amount of distilled water just prior to use.)

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FIG. 1

Equipment for filter paper electrophoresis.

6) A power supply, preferably 200 volts of direct current. (May be obtained by using ordinary wet cell batteries in series. However, a constant voltage power kit* can be purchased which will deliver the desired voltage when plugged into the usual 110 volt outlet.)

7) A saturated solution of amido black 10-B dye** in absolute methyl alcohol containing 10 per cent acetic acid.

The procedure consists of placing an equal amount of diluted buffer solution in each beaker. The positive and negative electrodes from the power source are then placed, one in each beaker. The ends of these electrodes should be wrapped in a small quantity of glass wool to minimize the spread of the intense pH change which takes place there. One of the glass plates is then bridged between the two beakers. The filter paper strip is prepared by first drawing a pencil mark across the center of it. It is then briefly immersed in the buffer solution and allowed to dry for a few minutes on a paper towel. Next the paper strip is placed on the glass plate with the ends dipping into the buffer solution in each beaker. The glass plate easily accommodates two or three strips for simultaneous determinations (one should be a known normal serum). A very small drop of serum is placed on the paper strip at the central pencil mark which serves as a reference point. The second glass plate is then placed on top of the paper and the current turned on. It is advisable to provide some sort of makeshift cover for this equipment to minimize evaporation from the beakers while the current is on. The current is allowed to run for about four hours after which time it is turned off, the glass plates separated, and the paper strips placed on paper toweling to dry.

When the paper strips are dry they are stained for 5 to 10 minutes in the amido-black solution. This is followed by three or four successive washes in beakers containing absolute methyl alcohol with 10 per cent acetic acid. Washing will largely remove stain from the filter paper leaving the dark blue stained protein components. The largest fraction, albumin, will be seen to have migrated approximately five cm. toward the positive pole. Migrating progressively less distances are the alpha$_1$, alpha$_2$, and beta globulins; the gamma globulin remains at the pencil mark representing the loading point, or perhaps migrates slightly toward the negative electrode.

*Available from the Heath Co., Benton Harbor, Mich., for $35.50.

**Available from the A. H. Thomas Co., Philadelphia, Pa.

Normal Alterations of Gamma Globulin in Early Life

There is evidence that the human placenta synthesizes gamma globulin but not albumin.[6] These studies correlate with certain clinical findings.[7] Fetuses of five months gestation or less have no gamma globulin. After six months gestation, however, gamma globulin begins to appear in the fetus and increases to the time of birth. It has been suggested that congenital agammaglobulinemia represents a persistence of a fetal pattern and that the level of gamma globulin may even be taken as an index of functional age of the premature infant.[8]

Newborn term infants have been shown to have gamma globulin levels slightly higher than those of their mothers. During the first month of life these levels decline to about one-third the level at birth, where it remains roughly stationary until 3 months of age. After this time there is a slow rise until adult levels are usually attained at 2 years of age.[9] Thus there is a period during infancy when a hypogammaglobulinemia, at least by adult standards, may be present which is actually physiologic.

Agammaglobulinemia

Since Bruton's initial paper[10] there have been several reports of children and adults with an almost complete absence of gamma globulin. While no gamma globulin can be demonstrated by electrophoresis, minute amounts can be detected in some instances by immunochemical methods.[11] Total proteins and albumin and globulin concentrations are often within low normal limits by routine salt fractionation or there may be slight reduction in the total protein with an elevated A/G ratio.

Most of the individuals reported with this syndrome have certain common characteristics. These include conspicuous susceptibility to bacterial infections, particularly with respiratory pathogens. However, these patients may have a normal response to common viral infections and vaccination with vaccinia virus.[12] The profound immunologic handicap interferes with their response to artificial immunization. These patients have an absence of known antibodies in their serum, including natural isohemagglutinins against heterologous groups when their blood types are O, A, or B. Neutropenia, which may be transient or cyclic, has been observed in many of these individuals.

Except for gamma globulin, protein formation is normal. Presumably the defect is one of failure of synthesis rather than accelerated rate of destruction since the half-life of passively transfused globulin is normal.[12] The pathologic lesion is thought to be a failure of plasma cell formation since they are the only cells lacking significant representation in the bone marrow.[13] Observations have shown a depletion of lymphoid tissue with absence of germinal centers and preplasma and plasma cells in lymph nodes even after antigenic stimulation.[14,15] Replacement therapy with 0.1 Gm. of human gamma globulin per kilo of body weight (0.3 cc. per pound) at monthly intervals protects these patients against many bacterial infections.

Congenital Agammaglobulinemia

The majority of cases of agammaglobulinemia reported in childhood are apparently congenital and hereditary in origin. These patients have all or almost all of the characteristics described above. All previously reported cases have been in males and therefore it has been postulated that this is a sex-linked characteristic.[16] The data from one family studied indicated that this abnormality occurred only in male members and was transmitted through unaffected females in a way similar to hemophilia.[17] The case to be reported here would indicate that this defect may not be a sex-linked characteristic affecting invariably only males.

Case 1. *Clinical Course.* C. C., a white girl, and first born, was delivered on February 12, 1952, following normal gestation. She had no difficulties until six and a half months of age when she had furunculosis associated with fever. A good therapeutic response was obtained with penicillin. At 10 months she was successfully vaccinated with vaccinia virus without any untoward complications.

Three months later the child again had pyodermia and had fever for five days. The white blood count was 10,050 with only 10 per cent polymorphonuclear cells. A blood culture showed no growth and the child responded well to penicillin therapy.

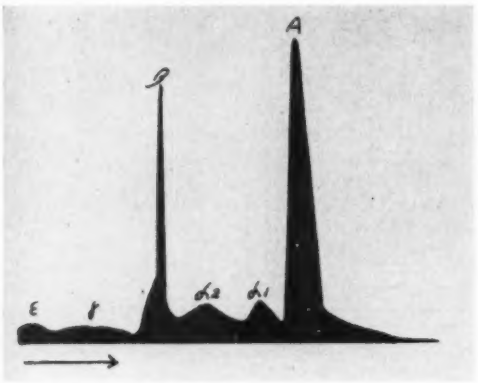
Fever recurred at 15 months of age. No abnormal physical findings were noted except slight abdominal distension and moderate axillary lymphadenopathy. Eight days after the onset of fever a firm edema was observed which was confined to both forearms. A diffuse thickening and hardening of the skin developed over this area. Ten days later a facial cellulitis appeared. The blood picture revealed an initial leukocytosis of 25,400 which gradually declined to 13,150, but this decline was associated with a progressive eosinophilia up to 19 per cent. The following tests were all normal: urinalysis, stools for parasites, Wassermann, blood sugar, calcium, phosphorus, phosphatase, blood culture, tuberculin and trichinella skin tests, and chest and skeletal x-rays. Sedimentation rate was 4 mm. in 1 hour (Westergren). The total protein was 4.6 Gm., with an albumin fraction of a 3.5 Gm. and globulin fraction of 1.1 Gm. per 100 cc. Biopsy of the indurated area over the forearm showed an atrophic pigmented epidermis and very dense collagenous tissue. There was no appreciable infiltration of inflammatory cells. Sections of muscle revealed no abnormality. The microscopic picture was felt to be quite compatible with scleroderma. •One month after biopsy the wound was still not healed and an abscess developed at the biopsy site. Gamma streptococci and *Staph. aureus* were cultured from this lesion. An aspiration of bone marrow was done on June 27, 1953; a careful review of this slide did not reveal the presence of any plasma cells.

During the next four months the child suffered from recurrent bouts of otitis media despite prophylaxis with penicillin. Cortisone given orally had no apparent beneficial effect upon the scleroderma. The child was hospitalized in November, 1953, because the fever, which had been low grade, became septic in type. Blood count then revealed a neutropenia of 3,850 with agranulocytosis. On three peripheral blood smears taken over a two day period no polymorphonuclears were seen. The sedimentation rate was only 7 mm. in 1 hour (Westergren). Hemolytic *Staph. aureus* were cultured from a vesicle that progressed to an abscess of the finger. Large ulcerating subcutaneous abscesses developed about the vulva and buttocks. *Aerobacter aerogenes* was recovered from a blood culture during this illness. Following blood transfusion and administration of four ml. of human gamma globulin she showed remarkable improvement within 36 hours. Temperature declined to normal, skin lesions began to heal, and polymorphonuclear leukocytes appeared in the peripheral blood. Despite a variety of antibiotics, however, a chronic left suppurative otitis media persisted.

Hepatomegaly was noted in April, 1954, and mod-

•Sections reviewed by Dr. J. L. Beven and A. L. McQuown of Baton Rouge, La., and Dr. Fred D. Weidman of the University of Pennsylvania who concurred in this opinion.

FIG. 2



(Case 1) Schlieren diagram.

TABLE 1

ELECTROPHORETIC ANALYSIS OF SERUM (CASE 1)

Date	Albumin %	Globulins Alpha$_1$ %	Alpha$_2$ %	Beta %	Gamma %	Total Protein Gm. per 100 cc.
11/30/54	63.5	7.4	8.8	18.2	2.1	7.06 (?)
12/ 2/54	64.1	8.2	8.8	14.2	4.7	QNS
1/29/55	61.7	9.7	9.4	16.3	2.9	5.26
3/12/55	63.9	8.1	6.9	17.3	3.8 (11-12 normal)	3.43

erate ascites was present. A cephalin flocculation test was negative. Corticotropin (ACTH) therapy had no appreciable effect upon the induration, which was now generalized, in the subcutaneous tissues. A recto-vaginal fistula appeared in July, 1954, and a pericardial friction rub was audible during the same month. An electrocardiogram was suggestive of some degree of pericarditis and a roentgenogram revealed slight cardiac enlargement. In September, 1954, the temperature rose to 105 degrees with recurrence of skin abscesses. The white blood count was 11,550 with only 3 per cent polymorphonuclear cells. Following administration of gamma globulin the child again became afebrile within 48 hours, skin lesions promptly healed, white blood count rose to 50,750, and granulocytes increased in the peripheral blood.

Since that time the patient has been maintained on 10 ml. of human gamma globulin intramuscularly every six weeks. She has been afebrile except for a bout of pneumonitis which responded rapidly to chloramphenicol and an additional dose of gamma globulin. Physical activity has increased and her disposition has changed from a chronically irritable individual to a happy child. Although she still has the clinical characteristics of generalized scleroderma the skin and subcutaneous tissues have become softer. A second skin and muscle biopsy from the pectoralis major done in January, 1955, showed only a slight increase in collagen in the dermis. The changes seen in the first biopsy were now practically nonexistent. An attempt was made during this biopsy to obtain an axillary lymph node for examination but no nodes were found available through the biopsy incision. A second bone marrow study done at three and a half years of age again failed to reveal the presence of a single plasma cell despite a count of several thousand cells.

Special Studies. Zinc turbidity test showed a reduced reaction to 1.5 units. The child has type-A blood but no anti-B agglutinin titer was demonstrable. Her antistreptolysin titer was negative. The Schick test was positive despite completion of routine D.P.T. immunization at 5 months of age. No measurable antibodies against vaccinia virus were present despite a primary vaccination take.*

Several electrophoretic studies of the patient's serum revealed extremely low values for gamma globulin and elevated levels for beta globulin (Fig. 2, Table 1). Because of the child's obvious dependence upon regularly administered human gamma globulin no electrophoretic pattern was obtained following an interval of longer than five and a half weeks after an injection of globulin. The measurable amounts of gamma globulin represent, at least in part, injected globulin. Radioactive tagged gamma globulin would give an accurate index of this fraction, but attempts to obtain a supply of tagged globulin failed. By calculation,** however, the portion of gamma globulin which represents injected globulin can be estimated.[1] The total gamma globulin determination of 130 mg. per 100 cc. on March 12, 1955, includes approximately 100 mg. per 100 cc. from injected globulin. This leaves an increment of 30 mg. per 100 cc. or perhaps less derived from the patient's tissues which is within the range usually considered necessary for true agammaglobulinemia.

Family Studies. Electrophoretic patterns of both parents and all four grandparents were essentially normal. A younger male sibling had a slight reduction of gamma globulin which probably was normal for his age. A still younger female sibling had a normal gamma globulin level at four days of age but a distinct reduction at four and a half months of age (Fig. 3, Table 2). This level may however represent normal values for the infant's age.[9,18] Both siblings have natural isohemagglutinins present, and both have been free of any recognized infections.

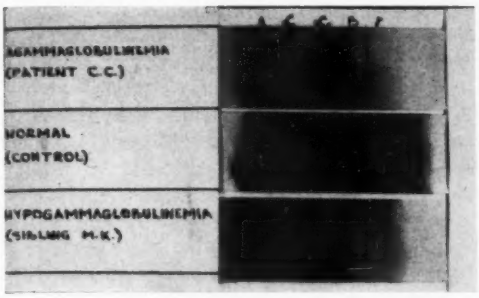
Acquired Hypogammaglobulinemia

Although the majority of such cases reported have been males there are reports of afflicted females and the syndrome is not considered sex-linked.[19] In some instances it has developed secondarily as a result of disease of lymphatic or reticulo-endothelial systems. However, in many instances the cause is unknown. Congenital agammaglobulinemia

*Courtesy of Dr. C. H. Kempe, University of California, San Francisco, Calif.

**The total mgm. of gamma globulin injected is divided by twice the plasma volume (10 per cent of body wt.). This figure represents the mg./cc. of gamma globulin present 3 days after administration. Within 30 to 60 days this increment drops by 25 to 50 per cent since the half-life of gamma globulin is 30 to 60 days.

FIG. 3



(Case 1) Filter paper strips.

is usually complete while the adult disease is often an extreme hypogammaglobulinemia.[13] An instance of this syndrome has been reported recently associated with a severe wound infection which failed to respond to any therapy until gamma globulin was given.[20]

Hypogammaglobulinemia Associated With Lowering of Other Serum Proteins

In starvation or the nephrotic syndrome gamma globulins as well as other serum proteins are low. It is well known that recurrent infections may constitute serious problems in these patients.

There are several reports of idiopathic hypoproteinemia associated with edema and low levels of gamma globulin.[21-23] Recurrent infections may not always be a problem in these patients even despite the failure to demonstrate humoral antibodies as suggested by Schick's observation.[21] An unexplained hypoproteinemia may be transient in nature perhaps because of some temporary derangement in protein synthesis and/or catabolism. Wyngaarden and associates[24] reported one patient with this syndrome in which there was edema, eosinophilia, and a transient lowering of plasma albumin and particularly gamma globulin. The following child presented similar findings to those he reported.

Case 2. W. H., a white girl, was apparently well until two and a half years of age. The only previous illness was one bout of otitis ten months before, associated with a mild hypochromic anemia which responded rapidly to simple iron therapy. Dietary intake had been apparently adequate before this illness. On October 13, 1953, she became apathetic and began to develop a generalized edema particularly in the periorbital areas. The liver extended two fingerbreadths below the costal margin and a moderate ascites developed. Body weight increased from 23 to 26½ pounds within five days. Blood pressure was consistently normal. Roentgenograms revealed an infiltrate in the left upper lobe which cleared within seven days.

TABLE 2

ELECTROPHORETIC STUDIES OF FAMILY (CASE 1)

Relationship	*Date*	*Total Protein Gm. per 100 cc.*	*Gamma Globulin %*
Paternal grandfather	1/29/55	6.70	13.3
Paternal grandmother	1/29/55	6.91	14.1
Maternal grandfather	7/ 1/55	Normal*	Normal*
Maternal grandmother	1/14/55	6.54	13.4
Father	1/14/55	7.79	13.9
Mother	1/14/55	4.67	12.9
	8/ 1/55	7.78	10.9
Male Sibling (Born 10/4/53)	12/ 7/54	7.0	10.2
	1/29/55	6.78	9.8
Female Sibling (Born 1/10/55)	1/14/55	4.69	11.2
	5/25/55	6.01	7.1
	8/ 1/55	7.43	8.9

*Reported from the Texas Children's Hospital.

Urinalyses were consistently negative and the urinary output seemed adequate. White blood counts ranged from 21,650 to 28,750 with an eosinophilia of 6 to 11 per cent. Sedimentation rate was 18 mm. per hour (Westergren). The following tests were normal: stool examinations, tuberculin and trichinella skin tests, heterophil antibody titer, cephalin and thymol flocculations, serum bilirubin, nonprotein nitrogen, blood urea nitrogen, and blood sugar. However, there was a remarkable reduction in total blood protein (Table 3). Electrophoretic patterns of the serum demonstrated that the greatest decrease was in albumin and gamma globulin fractions (Table 4).

Sixteen days after the onset of illness edema began to diminish as total protein rose. There was also a simultaneous decrease in eosinophilia. Subsequently the child has been well, without any undue infections.

Hypergammaglobulinemia

Elevated levels of gamma globulin may occur in Hodgkin's disease and malignant lymphomas,[25] multiple myeloma, impaired liver function, syphilis, tuberculosis, sarcoidosis, and leprosy.[4] Levels are also elevated in the active collagen diseases, and it has been postulated that pathogenetically these dis-

TABLE 3

FRACTIONAL PROTEINS (CASE 2)

Date	*Total Protein Gm. per 100 cc.*	*A/G Ratio*
10/20/53	2.4	2.3/0.11
10/23/53	2.85	2.17/0.10
10/25/53	3.32	2.07/1.25
11/ 5/53	4.42	2.86/1.56
11/10/53	5.14	3.16/1.98
12/ 9/53	7.21	4.49/2.72

TABLE 4

ELECTROPHORETIC ANALYSIS OF SERUM (CASE 2)

Serum Fraction	*10/27/53*		*11/14/53*		*12/12/53*	
	%	*Gm. per 100 cc.*	*%*	*Gm. per 100 cc.*	*%*	*Gm. per 100 cc.*
Albumin	38.37	0.82	43.05	2.27	49.02	2.66
$Alpha_1$ Globulin	11.42	0.24	8.54	0.45	6.41	0.35
$Alpha_2$ Globulin	19.29	0.41	15.99	0.84	12.84	0.70
Beta Globulin	17.59	0.38	14.26	0.75	11.64	0.63
Fibrinogen	8.48	0.18	6.22	0.33	7.82	0.42
Gamma Globulin	4.85	0.10	11.94	0.63	12.27	0.67
Total		2.13		5.27		5.43

eases represent dysgammaglobulinemias.[26] It has been suggested that the cause of collagen disease may be the production of abnormal gamma globulin from plasma cell proliferation.

Janeway and associates[27] reported five patients with hepatosplenomegaly, lymphadenopathy, normal antibody responses, and high levels of gamma globulin. Plasma cells were prominent in the tissues studied. Despite the high level of gamma globulin these patients suffered from recurrent infections of the skin or respiratory tract. Such patients have been observed by other workers. It has been postulated that perhaps these patients possess quantitatively high, but qualitatively poor gamma globulin. Some have apparently obtained benefit from administration of normal gamma globulin.

Comment

Abnormalities of gamma globulin are no longer merely medical curiosities but can be, and are, recognized with increasing frequency. Filter paper electrophoresis, although more limited in quantitative accuracy than the classical technic of Tiselius, has distinct advantages of simplicity and economy for screening at the clinical levels of office or outpatient practice. Certainly any clinical laboratory should be able to utilize this technic with a minimum of effort and expense, and it can be employed as any other office laboratory procedure with very little difficulty.

There does not seem to be much doubt that, as we gain more knowledge, determination of gamma globulin levels will have even more useful clinical applications. Perhaps the widespread use of antibiotics so early in life may alter immune responses to the extent that gamma globulin determinations may become almost "routine." A fertile field might be its use routinely in children with recurrent bacterial infections, particularly pyodermia and pneumonitis,[28] and in patients with infections refractory to antibiotics.[29]

The inference is drawn that the first girl presented (Case 1) represents congenital agammaglobulinemia because of its onset relatively early in life. Congenital agammaglobulinemia may be a sex-linked trait transmitted by females and occurring in males, and, just as in bonafide instances of hemophilia, this child may represent an isolated case in a female. However, a more likely explanation would be that this trait represents an autosomal recessive characteristic. The demonstration of the development of hypogammaglobulinemia in the female sibling from the time of birth lends support to the evidence of placental gamma globulin synthesis. Only continued follow-up gamma globulin determinations will answer the question whether this hypogammaglobulinemia is transient and physiologic or pathologic representing perhaps a single gene effect.

The ability to have a satisfactory vaccination without complication but failure to demonstrate subsequent presence of circulating vaccinia virus antibodies suggests that either the child had a relatively short-lived immunity or that recovery from vaccination took place without aid of these antibodies. Since these patients are reported to withstand viral infections well but do not produce antibodies after viral antigenic stimulation[13] perhaps prophylactic immunizations against viral infections, such as poliomyelitis, should be concerned with indices other than circulating antibody production.

The association of congenital agammaglobulinemia and generalized scleroderma also requires some speculation. During the most active phase of her scleroderma presumably the child also had agammaglobulinemia. However, an elevated beta globulin may be present. Perhaps this represents an abnormal globulin which would not be at variance with the belief that the common denominator in all collagen diseases is a dysgammaglobulinemia, or perhaps more correctly a dysglobulinemia. However, the failure to

demonstrate plasma cells in her bone marrow would tend to lead to considerable doubt that the common denominator in all collagen diseases is hypergammaglobulinemia from plasma cell proliferation.

The second child presented (Case 2) had findings identical to a previously reported child. This indicates there may be a syndrome consisting of the triad of edema, eosinophilia, and transient hypoproteinemia (particularly in the albumin and gamma globulin fractions).

Summary and Conclusions

1. Alterations in gamma globulin levels are being recognized with increasing frequency.

2. Indications for, and importance of gamma globulin determinations are pointed out.

3. Filter paper electrophoresis is a practical technic which can be employed as an office procedure for screening gamma globulin levels.

4. A case of agammaglobulinemia in a female infant with generalized scleroderma is presented.

5. This association casts some doubt on the hypothesis that the basic etiology of all collagen diseases is production of abnormal gamma globulin from plasma cells.

6. Apparently there is a syndrome consisting of the following triad: edema, eosinophilia, and transient idiopathic hypoproteinemia.

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References

1. Gitlin, D., and Janeway, C. A.: Agammaglobulinemia-Congenital, Acquired, and Transient Forms. To be published.
2. Oudin, J.: Serological Approaches to Studies of Protein Structure and Metabolism, New Brunswick, N. J., Rutgers University Press, 1954.
3. Stern, K., and Reiner, M.: Electrophoresis in Medicine, Yale J. Biol. & Med. 19:67, 1946.
4. Lewis, L. A.: Electrophoresis in Physiology, Am. Lect. Series Mono. 89, Springfield, Illinois, Charles C. Thomas, Publisher, 1950.
5. Kunkel, H. G., and Tiselius, A.: Electrophoresis of Proteins on Filter Paper, J. Gen. Physiol. 35:89, 1951.
6. Dancis, J., Broverman, N., and Katchin, B.: Synthesis of Serum Proteins by Human Placenta, Abstr. Comb. Meet. Am. Ped. Soc., etc., 1955, p. 37.
7. Sternburg, J., Dogenois-Perusse, P., and Dreyfuss, M.: Electrophoretic Studies of Serum Proteins in Normal and Pathological Newborn, Abstr. Comb. Meet. Am. Ped. Soc., etc., 1955, p. 178.
8. Martin, N. H.: Agammaglobulinemia—A Congenital Defect, Lancet 22:1094, 1954.
9. Orlandini, T. O., Sass-Kortsak, A., and Ebbs, J. H.: Serum Gamma Globulin Levels in Infancy, A.M.A. Am. J. Dis. Child. 84:632, 1952.
10. Bruton, O. C.: Agammaglobulinemia, Pediatrics 9:722, 1952.
11. Bruton, O. C., Apt, L., Gitlin, D., and Janeway, C. A.: Absence of Serum Gamma Globulins, A.M.A. Am. J. Dis. Child. 84:632, 1952.
12. Janeway, C. A., Apt, L., and Gitlin, D.: Agammaglobulinemia, Tr. A. Am. Physicians 66:200, 1953.
13. Good, R. A.: Agammaglobulinemia—A Provocative Experiment of Nature, Bull. U. Minnesota Hosp. & Minnesota Med. Found. 26:1, 1954.
14. Craig, J. M., Gitlin, D., and Jewett, T. C.: The Response of Lymph Nodes of Normal and Congenitally Agammaglobulinemic Children to Antigenic Stimulation, A.M.A. Am. J. Dis. Child. 88:626, 1954.
15. Good, R. A.: Studies on Agammaglobulinemia II Failure of Plasma Cell Formation in Bone Marrow and Lymph Nodes of Patients with Agammaglobulinemia, J. Lab. & Clin. Med. 46:167, 1955.
16. Good, R. A., and Varco, R. L.: Successful Homograft of Skin in Child with Agammaglobulinemia, J.A.M.A. 157:713, 1955.
17. Porter, H.: Personal Communication.
18. Knapp, E. L., and Routh, J. J.: Electrophoretic Study of Plasma Proteins in Normal Children, Pediatrics 4:508, 1949.
19. Zinnemann, H. H., Hall, W. H., and Heller, B.: Acquired Agammaglobulinemia, J.A.M.A. 156:1390, 1954.
20. Latimer, E. O., Fitzsimons, E. J., and Rhoads, P. S.: Hypogammaglobulinemia Associated with a Severe Wound Infection, J.A.M.A. 158:1344, 1955.
21. Schick, B., and Greenbaum, J. W.: Edema with Hypoproteinemia Due to Congenital Defect in Protein Formation, J. Pediat. 27:241, 1945.
22. Bound, J. P., and Hochett, W. R.: Idiopathic Hypoproteinemic Oedema and Amino-Aciduria in an Infant, Arch. Dis. Childhood 28:104, 1953.
23. Fried, C. T., and Henley, W. L.: Deficiency in Gamma Globulin with Edema and Hypoproteinemia, Pediatrics 14:59, 1954.
24. Wyngaarden, J., Crawford, J., Chamberlin, H., and Lever, W.: Idiopathic Hypoproteinemia, Pediatrics 9:729, 1952.
25. Arends, T., Coonrad, E. V., and Rundles, R. W.: Serum Proteins in Hodgkin's Disease and Malignant Lymphoma, Am. J. Med. 16:833, 1954.
26. Ehrich, W. E.: Immunity and Hypersensitivity Relationship to Disease in Man, Rep. Ninth M & R Ped. Res. Conference, 1955, p. 54.
27. Janeway, C., Craig, J., Davidson, M., Downey, W., Gitlin, D., and Sullivan, J.: Hypergamma-globulinemia Associated with Severe Recurrent and Chronic Non-Specific Infection, A.M.A. Am. J. Dis. Child. 88:388, 1954.
28. Collins, H. D., and Dudley, H. R.: Agammaglobulinemia and Bronchiectasis, New England J. Med. 252:255, 1955.
29. Harris, J. R., and Schick, B.: Use of Gamma Globulin in Infections Refractory to Antibiotics, J. Mt. Sinai Hosp. 21:148, 1954.

Discussion (Abstract)

Dr. Ralph Bowen, Houston, Tex.* Dr. Van Gelder has given us an excellent clinical review of the clinical significance of alterations in gamma globulin levels, but in his modest way failed to state specifically that this case is the first documented congenital agammaglobulinemia in a female as reported to date. It was my pleasure to see this child and her brother while visiting Houston. At Dr. Van Gelder's request this family was checked further and all findings parallel his report as substantiated by the following electrophoretic pattern.

In the literature, there are about 40 cases of agammaglobulinemia and one which had been considered to be a congenital case in the female has more recently been studied by Dr. Robert A. Good of Minneapolis, and his studies prove the case to be one of acquired agammaglobulinemia. She was well until she was 22 years old and showed no unusual susceptibility to infection and required no specific medical attention. Suddenly the situation changed and her life became one round of one severe bacterial infection after an-

*Deceased.

other. During the past 8 years, in contrast to her previous good health, she has had 34 attacks of pneumonia, bacterial meningitis on at least four occasions, recurrent otitis media, recurrent sinusitis and recurrent septicemia. On the basis of this history and on the basis of our thorough investigation of her hematopoietic system, we feel justified in classifying her along with other similar patients as a disease apart from that expressed by the children.

The symptoms in the children's disease usually are apparent during the second half of the first year of life when they become sick with pneumonia, meningitis, otitis, septicemia, septic arthritis, herpes zoster, and septic eczema.

And speaking of juvenile eczema, I would like to add a recent case shared with Dr. Lehmann of San Antonio who, after all measures had been tried and failed, made a dramatic response after being given gamma globulin. I am not inferring this is the answer for juvenile eczema, but where sepsis and infection occur it should be considered.

Dr. Van Gelder gave an excellent review of the various syndromes demonstrating the alterations of gamma globulin, but I would like to summarize a group of asthmatic children where gamma globulin studies were not altered, yet when used as a therapeutic agent had much to offer. In fact, it was like again finding the word "serendipity," which implies something not expected, or a pleasant experience exceeding expectations.

We are all familiar with this group who during the summer months do well, but in the winter periods, following marked changes in weather, complicated by respiratory infections, go down like dominos.

I gave 150 asthmatic children, between 1 year and 14 years of age, and alternate ones 5 cc. intramuscularly every month, starting in September, for the next 4 months. In a series of 1,200 injections of gamma globulin we never had a single systemic reaction.

The children receiving the gamma globulin had at least 50 per cent fewer attacks than the controlled group and showed less absenteeism from school, while in the control group 7 had to be hospitalized. I do not advocate this as a cure-all, but urge you try it in the asthmatic child. We found the Pitman-Moore, Lederle, and Cutters to be excellent gamma globulin and frequently pooled these.

One of the most inspiring reports was from Dr. Wm. A. Spencer, who is director of the Southwestern Poliomyelitis Respiratory Center in Houston, Texas. He had 10 respirator polio cases who were constantly troubled by respiratory disease. In spite of all antibiotic approaches no change was afforded. But after giving these patients large amounts of gamma globulin every four weeks for four months, their infections were for the first time brought to rapid conclusion.

As for electrophoresis studies, we have compared the two instruments, one which sells for $2,000, and the other for less than $100. The latter has proved very practical, but here again we should be qualified in the interpretation.

Also keep in mind that the absence of isohemagglutinins and comparatively slow erythrocyte sedimentation rate may afford a clue.

Some have raised the question about the positive Schick test as a criterion for gamma globulin need. Personally I believe it to be a false appraisal for we must remember that gamma globulin is a paradox and only gives a quantitative value and not a qualitative one.

Dr. Van Gelder is to be congratulated for such an excellent presentation and has reminded us of a new tool for improved characterization of many diseases and is to be most commended.

Contributions of Duke University School of Medicine and Duke Hospital*

EDWARD L. TURNER, M.D.,† *Chicago, Ill.*

This address was given at the Twenty-fifth Anniversary Celebration of the founding of Duke University School of Medicine and Duke Hospital.

IN A RECENT ARTICLE, Arthur Compton reminds us that according to the most generally accepted views of astronomers and physicists, the beginning of the physical universe dates from about four or five billion years ago. About three billion years ago the earth is believed to have been formed. The earliest evidences of life date back approximately a billion years. It is, however, within the past two generations of this vast expanse of time that many of the great developments of science and technology have occurred. These include such advances as the establishment of the germ theory of disease, proof of the existence of atoms, discovery of electrons and radioactivity, the development of knowledge of the age of rocks, the measurement of distance of stars and galaxies, the development of organic and biochemistry, the discovery of the sulfa drugs and antibiotics, and the discovery as well as extensive application of many forms of technology. He further comments that if we compare the five billion years of the existence of the universe to a year of time that these past two generations are the equivalent of a third of a second. But the remarkable fact is that during this equivalent of a third of a second there has been added to the heritage of man something that is substantial in relation to all of the long year of previous history.

In terms of time, the slightly less than one generation of the existence of Duke University School of Medicine and Duke Hospital is a very short period indeed. It has been during the generation when the most rapid changes in the known history of the universe have been taking place. In terms of institutional or human experience, however, the celebration of a quarter of a century of development is an event of genuine significance. To some individuals it might imply the development of aging with regrets that so much time has passed by. To some institutions it might indicate that to overcome the developed rut, stagnation and self-satisfaction that had been allowed to creep in, the time had arrived for that conflagration which a former university chancellor indicated might be a good thing for universities after twenty years of existence. On the other hand, to some individuals such an anniversary would be associated with a tremendous sense of appreciation of the exciting experiences and knowledge gained as well as the creation of a keen desire to forge onward with renewed vigor to the experiences and potential acquisition of knowledge in the years ahead. To an institution that has remained alive from its birth and that has deliberately planned to avoid stagnation or self-satisfaction such an occasion offers an opportunity to pause for a careful self-analysis. It is the time to take stock of accomplishments and to take pride in them. It is the time to attempt to project onward for even more fruitful years, as efforts are made toward improving those things with which there is current dissatisfaction.

It is not "peace of mind" or self-satisfaction that keeps individuals or institutions youthful. It is unrest, dissatisfaction with things as they are, eternal imaginative thought and genuine effort toward achieving greater and more perfect ends that keep them eternally youthful in outlook, progressive and thoroughly in tune with the rapidly changing panorama of life and time.

Duke University School of Medicine and Duke Hospital have maintained such an attitude from their beginning a quarter of a century ago and, as a result, celebrate at this

*Twenty-fifth Anniversary Address given at Durham on July 21, 1955.

†Secretary, Council on Medical Education and Hospitals of the American Medical Association.

time a silver anniversary of achievement justifying both youthful and mature pride. Knowledge and the wisdom to utilize it demonstrate the maturity that this youth has gained. Full awareness of the objectives of a medical school and teaching hospital that have been properly oriented with the basic reasons for their existence in this dynamic and rapidly changing panorama of human history have maintained youthfulness and vigor. Many another institution might well envy the record for it gives full promise of an even more exciting and productive period of achievement in the years ahead.

One cannot speak of a hospital and its contributions in a setting such as exists at Duke University without including the School of Medicine. After all, the Hospital came into existence because of the School of Medicine, and the two are so inseparably interwoven in their objectives and activities that my remarks are directed to both.

As I pondered over the subject matter of this address, I could not avoid an effort to search for the key factors which have led to the accomplishments and prestige that Duke University School of Medicine and Duke Hospital have achieved in their relatively short life span. Of course, the answer basically involves people. Leadership with imagination and foresight has been essential from the very beginning, for without such, basic planning and developmental coordination would not have been possible. This leadership Duke has enjoyed and it is to be congratulated on having been privileged to have had Dean Wilburt Davison at the helm and to have had associated with him administrators and teachers of outstanding qualifications and ability. Such leadership has made the relations between the School of Medicine, the Hospital and the University the kind of cooperative, understanding partnership essential to effective activity. I confess that I admire the concept of the Dean of the School of Medicine and the Superintendent of the Hospital that they consider themselves as adjutants to their faculty and staff, for an adjutant is an assistant and not a director or dictator or a passive figurehead. It is perhaps the attitude and philosophy expressed by the term adjutant that has emphasized the concept of partnership between faculty, hospital staff, students and administration in the history of this institution.

Apparently from the beginning this has resulted in unusually excellent cooperation and correlation in the planning of the curriculum and in the development of interdepartmental interests. In the summary of the report of the first official survey of Duke University School of Medicine and Duke Hospital in 1935, which is in the files of the Council on Medical Education and Hospitals of the American Medical Association, I find the following verifications of this impression:

"Duke University has made phenomenal progress during the first years of its existence. The outstanding features involve an unusually well trained faculty, relatively large departmental staffs and well planned curriculum. The activities of the various departments are very closely coordinated and a considerable number of faculty serve in both preclinical and clinical departments.

"The teaching of the preclinical departments is well correlated with the clinical subjects which are to follow and the teaching in the clinical departments is correlated back with the work of the preclinical departments.

"The medical course can be said to be a real cohesive one, aimed at a well rounded grounding in the fundamentals of medicine and in methods of approach to clinical problems."

Such comments in 1935 were more significant than they might seem to some of the younger teachers and staff members today. That was the period when there was still more or less rigid departmentalization in most of our schools of medicine. In many schools there was a distinct "gap" between the preclinical or basic medical sciences and the clinical departments. Students and many clinical faculty personnel felt the so-called "preclinical" subjects were essentially drudgery to be surmounted and left behind as rapidly as possible for the "real meat" that lay ahead in the third and fourth years of study. Although some clinical teachers were correlating and utilizing the subject matter of the preclinical years in their true sense as basic medical sciences essential to clinical understanding, many were not doing so in a significant manner. There was relatively little interest in, or effort made at cooperative interdepartmental planning. The curriculum in many institutions was a fairly static structure adjusted to a traditional pattern of years standing and almost considered sacred by some of the older faculty members.

True enough, efforts were being made in many schools to develop innovations in the curriculum as younger individuals well versed

in applied basic sciences began to enter the field of clinical teaching. It is not easy to readjust from tradition for, as Nietzsche stated: "Every tradition grows more venerable—the more remote is its origin, the more confused that origin is. The reverence due to it increases from generation to generation. The tradition finally becomes holy and inspires awe." Tradition need not, however, become the gremlin Arnold described when he wrote: "I am well satisfied that if you let in but one little finger of tradition, you will have in the whole monster, horns and tail and all." The real problem lies in knowing how and where to effectively utilize some facets of tradition and where to make sincere efforts to discard outworn methods in arriving at new concepts in keeping with changing times.

Duke University School of Medicine and Duke Hospital were fortunate a quarter of a century ago to have the opportunity to start out new without the handicap that tradition has developed in long established institutions. Having participated in the reorganization of two medical schools and in the initial establishment and development of a third one, I can wholeheartedly attest to the fact that the opportunities offered in the latter situation make it much easier to weigh and utilize past experiences and attempt to avoid undesirable traditional methods and concepts.

Duke's development verifies another vital key to a successful program which lies in the area of the intercommunication essential to sound and intelligent development of any difficult achievement. Because there has been close cooperation between administration, faculty, hospital, staff and students there has been an abundance of the intercommunication which Charles Victor Roman stated, "begets confidence." Friendship, understanding and cooperation grow with acquaintance. It is isolation that tends to accentuate differences and breeds dissention. In general, we tend to dislike what we do not understand and are antagonistic to those things that are strange. Sound, progressive development and action necessitate that intercommunication which begets confidence and understanding and leads to integrated and effective effort.

In my opinion the greatest contributions Duke Medical School and Duke Hospital have made to the profession and to the field of medical care lie in the products of its undergraduate, graduate and postgraduate educational programs. It was recognized at the outset that the true worth of an educational institution rests on the merits of its product, namely its alumni. True enough, medical care and the advance of knowledge through research are important, but they are component parts of a modern program of medical education. They are part of what it takes today to educate physicians so as to meet their challenges in the ever growing need for physicians and for medical service. They constitute, as well, part of the program necessary in the education and training of those young men and women who desire academic and scientific careers. Regardless of the ultimate objective, medical practice or an academic, scientific career or a combination of both, the same high standard of excellence in basic medical science and clinical training is essential.

Duke has kept its "feet on the ground" in recognizing that the chief reason for medical education lies in the need for physicians and for medical service. Its objectives have been consistently high so as to offer the best possible opportunities to meet this need. The administration and faculty are fully aware of the fact that today medical education faces serious and demanding challenges in meeting the needs of an ever changing situation and that what was satisfactory yesterday or today may fall far short of meeting the needs of the future. It is up to medical schools, their parent universities and responsible administrative leaders to be on the alert and to assume constantly the necessary leadership in finding adequate solutions to the dilemma presented by the need for more physicians and for better distribution of medical care.

The cultivation and teaching of medicine on a strictly scientific basis is the only sound professional education to offer medical students, regardless of their plans for the future. This must, of course, include wise indoctrination in the art of practice. I find myself rather deeply concerned at times when I visit a medical school and hospital where the objectives of the institution are glibly stated to be to educate physicians for general practice. Too frequently the impression is gained that the basic training offered should be something different, something less thorough and exacting than is needed by those who plan to specialize. There is no double standard of excel-

lence for basic medical education. In my opinion, it is exceedingly important that medical schools all endeavor to offer the strongest possible undergraduate indoctrination in medical education so that the young physician has a solid foundation on which to erect his graduate experience for either general (family) practice or a more narrow specialty.

It has long been my conviction that general practice has been underselling itself and that we in medical education have not given it the recognition its true status and challenges deserve. At the turn of the century a medical degree was "open sesame" to any and all fields of medicine and surgery. This is 1955 and in the interval conditions have changed very rapidly. Knowledge in science and its application to medicine has grown at a rate hitherto unknown. The entire panorama of medical diagnosis and care has changed in the quarter of a century since the birth of this institution. The education and training offered during its first years would be, in many aspects, obsolete today. Specialization has been a natural accompaniment of this vast accumulation of knowledge. It is necessary today and it is here to stay. Nevertheless, there is limited need for narrow specialization and the dominate need for medical service rests, and will continue to rest for a long time to come, in the area of general (family) practice. . The challenges in this field and how they can be met most effectively are matters of concern to all engaged in medical education.

Next to prevention of disease and disability, presumably the most important function of a physician is to be able to determine what is wrong with a patient so that intelligent therapy may be pursued. This approaches the basic function of an internist. One who plans to enter general (family) practice should, therefore, possess a sound indoctrination in the fundamentals of internal medicine. Such an individual is also expected to capably handle many aspects of pediatrics, normal obstetrics and certain simple emergency surgical situations. This individual must also possess full awareness of his limitations and be the first to seek the aid of the specialist when indicated. Instead of a challenge that is something less than that of the specialist, it is my opinion that we should recognize adequate general (family) practice as something that offers a broader and more demanding challenge than the narrower specialties. I have been thoroughly convinced that in graduate and postgraduate areas of education our cloth should be cut more in keeping with the pattern demanded by such a challenge. In this area graduate medical education has been "dilly-dallying" for it is utter nonsense that in some places a year of rapidly rotating or "vibrating" internship is considered to be all that is needed to accomplish the desired end. Some internships still rotate on the monthly basis as if 30 to 31 days represented a magic period of educational opportunity regardless of the service or experience involved. Rotating internships may give good experiences if the rotation is reasonable and in keeping with the relative importance of the services offered. I know many, however, where the rotation is based on administrative convenience and hospital service factors rather than on logic, continuity of experience or educational value to the house staff.

It would seem that a minimum two year "mixed" or "rotating" graduate experience such as Duke has offered in the past is a more logical approach today toward meeting general over-all needs. Certainly a straight initial graduate experience in almost any field would offer a preferable experience in contrast to the "vibrating" type where rotation is too rapid to permit any continuity. Here is where some careful study might result in a re-evaluation of the basic training needs in specialty areas and ultimately result in some healthy modifications in specialty training requirements. Specialty Boards have become involved in the fetish of time requirements rather than in the more important factors of content and experience.

In discussing this interesting area of medical activity, I have digressed somewhat from the main current of thought. It is interesting, however, as well as gratifying to note that over forty per cent of the graduates of Duke University School of Medicine indicate a desire to enter the field of general (family) practice. This implies that the undergraduate experience in medical school has included contacts in the clinical years of study which have given perspective as well as due emphasis on the importance of preparation for both general (family) practice and narrower specialization.

In all fairness, it must be recalled that the trend toward specialization in recent years

has been given great impetus by the treatment afforded physicians in the various Federal Services. Preferential consideration has been given to those who possessed the little piece of paper signifying certification. These little pieces of paper are important today, but it must always be remembered that they attest to only certain assets of the total individual who possesses one of them. It was not surprising that there was a deluge of discharged medical personnel who sought such certification as soon as they were released from service. It should not be surprising either that the young medical graduate today has caught the fever of specialization and desires what is frequently represented as an easier existence than that associated with general (family) practice. There are many ways, however, through partnership and group practice arrangements whereby family practice may be made a more satisfying and less strenuous adventure than it might otherwise become.

Duke Hospital has contributed a vitally important role in its partnership in making available the facilities for the medical care essential to all phases of medical education. Its record is a fascinating one as it has grown in prestige throughout the years. The methods utilized in overcoming the public abuses sometimes accompanying charity offer a logical common sense pattern for other institutions. Mr. Altvater's experiences as Superintendent, in the early thirties when he demonstrated that most of the patients paying nothing could pay part, if not all of their expenses, is reminiscent of an experience I had during the same period while on the staff of the American University of Beirut in the Lebanons. Outpatient fees at that time were nonexistent. The Arab and Bedouin patients from the interior who frequented the clinic seemed to accept something that cost nothing as worth the same value. Some of us advised developing a fee schedule in accord with the ability of patients to pay. It was interesting to observe the change in the patients' reactions, even though they paid only a few piasters, during the course of the next year or so. Payment, though in many instances not in excess of the equivalent of a bus token, nevertheless, represented payment for something and that something then had value and respect. Getting patients to follow through with their diagnostic or therapeutic instructions took a definite trend to the good. Increased financing through this source also made it possible to conduct improved services. When the "chips are down" most people desire at least self-respect which is largely lacking in those who falsely seek charity. Charity where honestly needed should continue to be a virtue of physicians and hospitals, but the abuses so frequently accompanying it should be zealously counteracted.

The development of the inclusive or flat hospital rate for pay patients which Duke Hospital introduced in the early thirties was an interesting and significant step in view of subsequent developments in the field of hospital insurance. Duke has pioneered in this important national trend in the role played in introducing the inclusive or flat rate and in the organization of the Hospital Care Association in the early thirties. These were early and basic developments in the background of the advances that have more recently taken place in the field of prepaid medical care in the United States and from which both the patients and the hospital benefit today.

As medical knowledge increases in its scope, the needs for constant research and continuing educational opportunities for physicians as integral parts of the over-all program of the School and Hospital are ever more apparent. In research the faculty of Duke University School of Medicine has constantly been productive and currently the institution possesses a budget from special grants for research which almost equals its basic educational budget. To the administration and to Duke alumni this represents an expression of confidence in the caliber of the personnel who can command such support for their efforts in search of new knowledge. To the University administrators and to the adjutants of the School of Medicine and the Hospital this abundance of financial support for research is not an unmixed blessing, for it carries an important warning. In a thoroughly excellent school of medicine and a teaching hospital research must never be conducted to the point where it interferes with or minimizes the basic educational function of the institution. The training of physicians to meet the needs for physicians and for medical care must always be maintained as the primary area of concern. Research should and must enhance this function and in no sense replace it.

Postgraduate medical education today is assuming ever greater importance. Physicians currently obtain their postgraduate experiences in a variety of forms. In the survey of Postgraduate Medical Education recently made by the Council on Medical Education and Hospitals, there was ample support for the conclusion that medical schools and their teaching hospitals are destined to undertake greater and greater interest and activity in this field of continuing education. Duke has been active in this field and has contributed valuable postgraduate experiences through its course offerings and in the continuous postgraduate program for physicians in the area surrounding Duke Hospital.

As one surveys this active and productive period of approximately a generation there is reason for those who have participated in it to take pride in accomplishment. Furthermore, there should be reason to take some satisfaction that this institution has not gone through a cycle of development, reached the crest and then in smug satisfaction slid slowly behind in the competitive race for excellence awaiting new and younger blood to initiate a rebirth. This has been observed in more than one institution that started out with great promise within the memory of many of those present today. The youthfulness and potentialities of Duke University School of Medicine and Duke Hospital today exist because the period of self-satisfaction and smug complacency has been avoided through sound and imaginative leadership, wise intercommunication and intelligent partnership.

As the future is faced, all medical schools and their teaching hospitals must frankly evaluate the existing and potential challenges that constantly confront them. They lie in eternal re-evaluation of what is being done in endeavoring to determine how methods and technics as well as content should be readjusted to achieve more satisfactory ends. There is no time for sitting back and deciding with finality, for in this rapidly changing picture there is no such thing as finality. The whole world is changing about us, social and economic advances are as surely affecting the medicine of today and of the future as are the advances gained in scientific knowledge. There is work to do in re-evaluating and aiding in the readjustment of premedical education and in constantly analyzing and readjusting medical education in line with current needs. There is need for greater attention, planning and action in the area of graduate medical education and in the continuing opportunities that should be available in postgraduate medical education. The problems of better medical care, better hospital care and better distribution of medical services constitute further facets of current and future challenges. Study and an effort at guidance toward a reasonable balance in specialty fields, problems of interprofessional relations with other groups in areas such as nursing, technical fields and other ancillary personnel participating in certain aspects of medical diagnosis and care constitute further aspects of the challenge ahead for those in medical education. Administrative leaders and teachers have need of real imagination in planning for the future. But as Northead has stated, "Imagination is a contagious disease. It cannot be measured by the yard or weighed by the pound, and then delivered to the students by members of the faculty." Progress will be determined and communicated by those who wear their learning with imagination.

There is never much to fear in facing the future if the sights are set high and constantly worked for even though full attainment may not be achieved. Some years ago in his address on "America's Fitness for Survival" James B. Conant included a comment which I should like to pass on as equally applicable to the fitness for survival of Duke University School of Medicine and Duke Hospital. "Objectives can never be fully attained," he stated, for "they represent goals toward which men and women may move by concerted actions. They never can be reached in practice—almost by definition because they are ideals—but we can readily recognize whether we are moving toward them or retreating. . . . Ideals like stars can never be reached. But we use them to chart our course."

Present Status of Allergy in the Connective Tissue Diseases*

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The author reviews some of the present-day concepts of the etiology and pathogenesis of the so-called collagen diseases.

Introduction

THIS TOPIC IS PROPOSED for discussion with full realization that the concept of allergy or hypersensitivity as the basic etiologic factor in the so-called collagen or connective tissue diseases is by no means new or unpopular. The possibility of such a cause for rheumatic fever was expressed as early as 1913.[1] Furthermore, there is no intent to champion this hypothesis, but only to present the evidence both for and against, in order that recent important experimental findings and clinical data can be properly evaluated and correlated. It has been facetiously stated that the specialty of allergy can be chronologically divided into two periods,—B.C. and A.C.,—meaning, of course, "before cortisone" and "after cortisone."

It is now "7 A.C.," or seven years since the first patient with rheumatoid arthritis was successfully treated with cortisone, and yet "the fundamental basic mechanism of allergy is still unknown"[2]—as well as the modus operandi of the adrenal steroids in altering tissue reactivity. Nevertheless, it is instructive to summarize the various theories and current thinking in a general way and to recapitulate progress to this point.

The term "allergy" was first used by von Pirquet in 1903 and was meant to infer "altered reactivity," after exposure to or contact with foreign substances.[2] It has been generally accepted also that the term "allergy" may be used interchangeably with "hypersensitivity" and "hypersensitiveness."[2] The allergic response in the past has been held as primarily "a protective reaction" and a temporary disturbance in normal physiologic processes.[3] Such reactions have been assumed to be reversible and to represent a disturbance of function rather than organic pathologic change. All hypersensitive reactions therefore would be of this type, with the possible exception of anaphylaxis, which has always connoted a potentially fatal outcome. Experimental anaphylaxis and human allergy are indistinguishable, except in the degree or severity of response in various shock organs.[2] The classification of the various types of hypersensitive reactions and the terminology were difficult problems to early workers because of the lack of fundamental physiologic, immunologic and pathologic data. The problems created by antigen-antibody reaction were perhaps the best understood, and little progress in clarification was being made until the advent of the antihistamines and finally of the adrenal cortical steroids. For the first time agents were at hand which would arrest hypersensitive reactions regardless of fundamental cause, and at the same time were astoundingly effective in the amelioration or arrest of progress in a group of diseases of unknown etiology which had been designated as the "collagen tissue diseases."

In a recent article[1] concerning collagen tissue disease in general, it is stated that "in the six year period of 1941 to 1947 there were only two references in the Index Medicus to articles on this topic; during the next six years there were more than 120." Classified in the "Current List of Medical Literature" under the term Collagen Diseases are listed the following: rheumatoid arthritis, dermatomyositis, lupus erythematosus, periarteritis nodosa, rheumatic fever, rheumatism, and scleroderma. There are those who would include also thromboangiitis obliterans, ulcerative colitis, purpura, erythema nodosum, glomerlonephritis, serum reactions, drug sensitization,

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blood group incompatibility, temporal arteritis, malignant hypertension, endocardial fibroelastosis, thrombotic micro-angiopathy, and others.[1]

Historical Development of Concept of Connective Tissue Disease

Johannes Muller in 1834, was the first to use the actual word connective tissue after Bichat introduced the biologic concept of various tissues as functional units. He even went so far as to suggest that each tissue of the body reacted to stimulation in a more or less uniform manner irrespective of location, and promoted the idea that local diseases affecting particular organs were also accompanied with systemic diseases involving every type of tissue. Revival of interest in pathologic changes in connective tissue after Virchow's era of cellular pathology has only occurred in the last twenty-five years, and this renewed investigation came about as a result of elementary studies in rheumatic fever. Weintrand, in 1913, was the first to promote the idea that rheumatic fever itself might be an allergic disorder. Finally, in 1929, Klinge published his first paper concerning the possibility that the fundamental lesion in rheumatic fever was actually a mucinous edema and disruption of ground substance. His pathologic description of the primary lesion was degeneration of connective tissue fibrils and formation of fibrinoid degenerative masses. Furthermore, Klinge as early as 1929 found connective tissue lesions similar to those in rheumatic fever to be present in rabbits made hypersensitive to foreign proteins and thus came the first conclusion that fibrinoid degeneration of connective tissue was actually a characteristic lesion of tissue hypersensitivity. This work antedated by 13 years the classic experiments of Rich and Gregory at Johns Hopkins. In 1933, additional conclusions were drawn by Klinge that his experimental lesions in hypersensitivity were similar to those of polyarteritis nodosa and, since fibrinoid change was present in a number of other diseases, he included dermatomyositis, malignant hypertension, nephritis, acute bacterial endocarditis and thromboangiitis obliterans. There was initially wide acceptance of this most attractive hypothesis and it received a further enthusiastic support in 1937 by Clark and Kaplan's demonstration that such fibrinoid change was found in cardiac and connective tissue manifestations of serum sickness, and in 1938 when Masugi and Yä demonstrated that in diffuse scleroderma there was also a similar change in the blood vessels in this particular condition.[1]

Opponents of the allergic etiologic concept of the collagen tissue disease began to appear among the investigators of disseminated lupus eryhtematosus, which had not been included in the above group of diseases, except for the single suggestion by Stokes in 1922. Libman and Sacks published their monumental work and description of the cardiac lesions in 1924, which initially led to the change in viewpoint as to the etiology in this particular disease. The Mount Sinai group, consisting principally of Klemperer and Baehr, propounded the theory that the fundamental lesion was actually endothelial in site and all tissue damage was of fundamental vascular origin. The exact cause of this angiopathy, however, was not known and the specificity of the lesion was questioned by many and, in 1941, on re-examination of their material, the Mount Sinai group renounced this viewpoint and proposed the fundamental tissue change to be actually disturbance in the collagenous tissue. However, they were vigorous in their objection to the acceptance of the allergic cause, or even the assumption that there was tissue hypersensitivity in spite of the presence of fibrinoid change.[1]

About this time the electronic microscope and micrograms of collagen fibers first appeared in the work of Hall, Jakus and Schmitt, and this tremendous advance in the field of molecular biology began to provide more details in the study of the actual tissue degeneration. The description of hyaline, fibrinoid and amyloid degeneration by Oberling proved that connective tissue was involved and that precipitation of proteins by enzymatic agents resulted in the appearance of such degeneration.[1]

Quite rapidly during the next seven years detailed study of hypersensitivity reactions in tissue began to appear, and perhaps the most important of these was the work of Rich and his associates[4] at Johns Hopkins. Vascular lesions indistinguishable from those of periarteritis nodosa were found in the viscera of five patients who shortly before death had had

hypersensitive reactions following therapeutic injections of foreign serum and, of these five, four had received sulfonamides. The fifth patient had experienced serum sickness and no sulfonamide therapy. Because the lesions were fresh and none of the patients had symptoms suggestive of periarteritis prior to their terminal illness, Rich[4] concluded that such vascular lesions could be on the basis of anaphylactic type of hypersensitivity. In 1943, Gregory and Rich[5] published their findings in the experimental production of anaphylactic pulmonary lesions similar to those seen in rheumatic pneumonitis and, in 1943, the two investigators[6,7] had likewise produced lesions indistinguishable from those found in rheumatic carditis by anaphylactic produced hypersensitivity. Previously the lesions of periarteritis nodosa had been induced also by experimental anaphylaxis.[8] As a final touch, in 1945, Rich[9] reported hypersensitivity to iodine as a cause of periarteritis nodosa. The experimental animals used in most of this work were rabbits. In 1947, the last work appeared which demonstrated anaphylactic lesions of coronary arteries experimentally produced in rabbits which were said to be similar to those found in rheumatic fever and disseminated lupus erythematosus.[10] Perhaps the most significant contribution of all the work of Rich has been broadening the concept of the pathologic features of tissue hypersensitivity, and the results of anaphylaxis. The vascular or endothelial damage and lesions of the collagen tissue can be demonstrated as is characteristic of local tissue hypersensitivity.[1]

Then, in 1949, the reports of the effect of ACTH in rheumatoid arthritis, rheumatic fever, lupus erythematosus, dermatomyositis, scleroderma and polyarteritis nodosa first appeared and great were the expectations. The mode of action of the adrenal hormones still remains a puzzle. The response of all tissues to any noxious agent can be modified to a greater or lesser extent, leaving the underlying causes unaffected. This has been demonstrated experimentally both in humans and animals. An excellent review of the clinical and experimental action of the adrenal corticosteroids was presented before this section one year ago by Mayer.[11] One such promising faculty is the inhibition of the action of hyaluronidase which increases tissue permeability. Such increase in permeability also occurs in inflammatory reactions of any type and this concept might possibly explain the anti-inflammatory and anti-allergic effect of cortisone.[1] In 1952, Rawlins[12] propounded this theory as being fundamental in all allergic reactions. It was stated that hyaluronidase is markedly increased in all allergic skin reactions and is available in copious amounts in or near connective tissue gel. He assumed that there was a constant equilibrium in the enzyme system which forms and disrupts hyaluronic acid. In so-called nonallergic individuals there would be a constant normal amount of firm, stable, connective tissue gel. It is assumed that such stability in the enzyme system and the balancing of concentration of enzyme in or near the connective tissue is under the primary control of the autonomic nervous system. Localization of allergic reactions would then be predetermined by it.[12]

A much more ambitious and perhaps even more logical detailed theory had been previously proposed by Jaros,[13] in 1951. His hypothesis was founded upon the interrelationship of epinephrine, acetylcholine and histamine with the interplay of the enzymatic system, the adrenal corticoids, hypothalamus and autonomic nervous system.

Histamine. It is generally accepted that histamine is liberated at all cellular or tissue injury and that such injury may be on the basis of antigen-antibody reaction, trauma, infection, stress, physical factors, such as, light, heat and cold, and emotions. Hypersensitive individuals have a diminished tolerance for histamine and it is, of course, fundamentally parasympathomimetic in stimulating action. It may produce an eosinophilic leukocytosis and experimental animals shocked by this agent show lesions similar to arteritis and myocardial degenerative effect.[13]

Acetylcholine. This is an agent similar to histamine in many respects. It is produced throughout the entire body and of course is primarily involved in the transmission of nerve impulses. Large doses, however, may produce lesions similar to those seen in anaphylactic shock and experimentally it may produce vascular lesions similar to those of histamine itself. Of important interest is the large amount of high blood level of acetylcholine in patients with extreme degree of

hypersensitivity, such as, in status asthmaticus and in connective tissue diseases. To further enhance tissue entry perhaps it also induces the release of histamine. It is stated in this particular hypothesis that the acetylcholine serves only to stimulate the output of epinephrine, and that the peripheral effect of acetylcholine and histamine is mediated perhaps through the autonomic nervous system by way of the hypothalamus and the adrenal medulla.

So ends the so-called catabolic phase of Jaros'[13] hypothesis. In 1948, Farber and his co-workers[13] showed statistically that about 25 per cent of all allergic patients had low 17-ketosteroid output and that about 50 per cent of all asthmatic patients had high blood potassium values and one-third had low sodium and chloride blood levels.[13] Because of heredity, Jaros believes that in the hypersensitive patient more of the epinephrine goes to form acetylcholine and histamine than to stimulate the anterior pituitary for adrenal corticotrophic hormone release. The importance of adrenal cortical balance as far as steroid activity is concerned, is emphasized by Jaros. For example, desoxycorticosterone and desoxycortisone may produce widespread connective tissue proliferation, hyalinization of glomeruli, salt retention, rise of blood pressure, panarteritis and myocarditis, all lesions found in hypersensitive states, severe allergic reactions and in collagen diseases. On the other hand, cortisone or allied compounds or glucocorticoids cause a lysis of fibroblastic and collagenous tissue, and abolish the hypertension produced by desoxycorticosterone, and reduce the sodium and chloride blood levels. Jaros has promoted the idea that the peripheral beneficial effect of ACTH and cortisone on hypersensitive states is fundamentally carried out by the enzyme corticoids from the adrenal medulla. These are released by ACTH itself and result in the production of histaminase which quantitatively destroys histamine. This enzyme, of course, occurs in abundance in the lungs, kidneys, spleen, adrenals, and blood, and in all tissue; perhaps the placenta contains the most and in pregnancy the peak level is reached about the seventh or eighth month. As a corollary cholinesterase accelerates the destruction of acetylcholine, and the other enzymes, anti-hyaluronidase and glucuronidase, further increase the chances of inhibition of peripheral damage in hypersensitive states. So ends the anabolic phase of the hypothesis.

Proceeding from the establishment of this hypothesis, Jaros then discussed the pharmacologic actions of various drugs which have been found to be effective in allergic reactions and hypersensitive states of all types.[13] This was indeed an ambitious theory with just enough basic informative background to add to its attractiveness. Future developments may further substantiate his claim.

The antagonists of the allergic theory of all connective tissue diseases, and especially of lupus erythematosus, have leaned heavily on the specific phenomena known as the "L.E." cell, first discovered in 1946 by Hargraves and subsequently produced *in vitro* by Haserick and Borst in 1949.[14] Haserick proved quite clearly that the phenomenon was due to the presence in the plasma of lupus erythematosus of some particular agent which could produce the amorphous blue mass engulfed or phagocytized by the leukocytes from nuclear material and that this particular agent was carried in the gamma globulin fraction of serum protein and was antigenic.[14] However, typical "L.E." cells have been found in instances of severe drug hypersensitivity and other possibly unrelated entities, such as, pernicious anemia in relapse, dermatitis herpetiformis, multiple myeloma, hemolytic anemia, miliary tuberculosis, during cortisone withdrawal, and hydralazine (Apresoline) toxicity.[15] The most detailed study of positive "L.E." cells in patients without lupus erythematosus has been that of Welch and Zimmerman. In six patients with penicillin hypersensitivity there were three with severe reactions. All three of these had positive "L.E." (bone marrow) preparations from ten days to three weeks after the beginning of sensitivity reaction. Less specificity of the "L.E." phenomenon for disseminated lupus and more for hypersensitive states in general may be forthcoming.

Adding further difficulty in the acceptance of disseminated lupus erythematosus as a clinical entity has been the production in patients of a mirror image reversible syndrome by the administration of hydralazine. Obviously the importance here is the experimental production for the first time in humans of any collagen tissue-like disorder.[16]

In the beginning of 1955 probably the most popular hypothesis concerning a common causative factor in the collagen tissue diseases was that of the production of abnormal gamma globulins by Ehrich[1] in 1952. This was based on the increase in gamma globulins usually present in these diseases after considerable duration and the demonstration of the Haserick factor (a protein with specific antigenic properties) in the gamma globulin fraction of the plasma. To date, most investigations concern alteration in serum proteins with production of antigenic agents as the basic mechanism.

Final Summary and Correlation

From the sifting of the above material, it is apparent that established allergic diseases are necessarily associated with hypersensitivity and that there is evidence even more so of the hypersensitiveness in the connective tissue diseases. It is easy to classify hay fever, asthma, urticaria, etc., as "simple" hypersensitive states, yet frequently their management is indeed complex. The situation here is analogous to that existing in hypertension. It is better to offer the word "benign" in the sense that the allergic reaction is reversible in its primitive or initial forms and there is no *demonstrable* (by modern tools) pathologic or physiochemical permanent disturbance in the host. With repeated occurrence of altered tissue sensitivity, no matter what the primary cause, there may result the "malignant" phase of allergic reactions with connective tissue degenerative changes which, depending upon the particular shock organ, result in the various manifestations of connective tissue diseases. Furthermore, at the onset of any severe type of hypersensitive reaction, be it serum sickness or otherwise, there clinically can be progression into one form or another or a combination of the usual manifestations of connective tissue disease.

The causes for the "benign" becoming "malignant" hypersensitivity are the crux of the problem (in the same manner as in cellular mitosis and cytologic malignancy in general) be it repeated trauma, adrenal cortical exhaustion, change in gamma globulin with formation of antigens, enzyme system imbalance, and the like.

Of practical importance to the allergist, Kampmeier and Smith[17] have shown that diffuse arteritis may be a recurrent disease in the same patient, may exhibit several different forms of allergy, and finally connective tissue disease of different morphologic types. Thus "malignant" hypersensitivity may masquerade as "benign," and to add to the confusion, most consultations seen by the allergy specialist have had generous amounts of adrenal hormone. Refractiveness, presence of "L.E." cells, hyper- or dysglobulinemia, abnormal urinary elements and, best of all, a meticulous chronologic history may help clarify the picture. Good allergy practice remains detection of, removal of, if possible, or hyposensitization to offending agents producing hypersensitivity, thereby preventing a "benign" becoming a "malignant" problem. The judicious use of adrenal hormones involves delaying their exhibition until a diagnosis as exact as possible can be made.

Conclusions

1. Allergic and connective tissue diseases have hypersensitivity in common.

2. Their relationship, if any, is unknown because the basic phenomena in both diseases are also obscure.

3. The discovery of adrenal corticosteroids has to date been of no assistance in clarifying the issue.

4. Several current hypotheses have been reviewed.

5. The allergic concept of connective tissue diseases should in no way retard further attempts to identify each as a specific clinical entity and search for another causative agent.

Case Reports

Case 1. Mrs. B.M., age 65. The history and findings were those of: urticaria, angioneurotic edema, arthritis, progressive muscular weakness and wasting, erythema nodosa, nephritis with hematuria and albuminuria, cardiac hypertrophy and pericarditis, eosinophilia and presence of "L.E." cells; 1953 through 1955. Skin, muscle biopsy: *Dermatomyositis*. Kept on a maintenance dose Meticorten.

Case 2. Mrs. J.S., age 37. Symptoms and signs included: tenosynovitis and bursitis, 1951; anemia and increased CSR; arthritis, typically rheumatoid, acute in 1953, treated with gold and cortisone therapy; subcutaneous rheumatoid nodules and thrombotic arterial necrosis of left heel late in 1952; acute pleuritis and pulmonary infarction controlled only by large doses of cortisone. In 1955, besides refractory anemia, there were rapid CRS, periodic hematuria and albuminuria,

and one positive "L.E." cell preparation. Skin, muscle biopsy: *Negative.* At present no adrenal hormone is required. *Diagnosis:* Rheumatoid arthritis and variant connective tissue disease.

Case 3. Mrs. J.W.D., age 42. She has a history of allergic rhinitis, perennial with seasonal exacerbation for 30 years, migraine and urticaria for 15 years, and erythema multiforme in 1946. There was a cerebral vascular accident without residua in 1948. Migratory polyarthritis in 1953 was treated with cortisone. There were rheumatoid arthritic changes. In 1954, skin, muscle biopsy: *Connective tissue changes consistent with collagen disease.*

References

1. Robb-Smith, A. H. T.: The Concept of the Collagen Diseases, Practitioner 173:117, 1954.
2. Hansel, F. K.: Clinical Alergy, St. Louis: The C. V. Mosby Co., 1953.
3. Vaughn, W. T., and Black, J. H.: Practice of Allergy. St. Louis: The C. V. Mosby Co., 1948.
4. Rich, A. R.: The Role of Hypersensitivity in Periarteritis Nodosum as Indicated During Seven Cases Developing During Serum Sickness and Sulfonamide Therapy, Bull. Johns Hopkins Hosp. 71:123, 1942.
5. Rich, A. R., and Gregory, J. E.: On the Anaphylactic Nature of Rheumatic Pneumonitis, Bull. Johns Hopkins Hosp. 73:465, 1943.
6. Rich, A. R., and Gregory, J. E.: Experimental Evidence that Lesions with the Basic Characteristic of Rheumatic Carditis Can Result from Anaphylactic Hypersensitivity, Bull. Johns Hopkins Hosp. 72:239, 1943.
7. Rich, A. R., and Gregory, J. E.: Further Experimental Cardiac Lesions of the Rheumatic Type Produced by Anaphylactic Sensitivity, Bull. Johns Hopkins Hosp. 77:43, 1945.
8. Rich, A. R., and Gregory, J. E.: The Experimental Demonstration that Periarteritis Nodosum is a Manifestation of Hypersensitivity, Bull. Johns Hopkins Hosp. 72:65, 1943.
9. Rich, A. R.: Hypersensitivity to Iodine as the Case of Periarteritis Nodosum, Bull. Johns Hopkins Hosp. 77:43, 1945.
10. Rich, A. R.: Experimental Anaphylactic Lesions of the Coronary Arteries of the "Sclerotic" Type, Commonly Associated with Rheumatic Fever and Disseminated Lupus Erythematosus, Bull. Johns Hopkins Hosp. 81:312, 1947.
11. Mayer, Lloyd D.: An Experimental and Clinical Evaluation of the Corticosteroids in Allergy, South. M. J. 48:870, 1955.
12. Rawlins, A. G.: Hormonal-Connective Tissue Mechanism in Allergy, Ann. Allergy 10:440, 1952.
13. Jaros, S. R.: A Hypothesis on the Physiochemical Pathogenesis of Hypersensitivity States and Collagenous Diseases, Ann. Allergy 9:133, 1951.
14. Dowling, G. B.: Lupus Erythematosus, Practitioner 173: 140, 1954.
15. Jacobs, A. Gerson: A False-Positive Lupus Erythematosus Test, Ann. Int. Med. 42:1097, 1955.
16. Desten, H. P., Taylor, R. D., Corcoran, A. C., and Page, I. H.: Syndrome Elicited by Prolonged Administration of Large Doses of Hydralazine, J. Lab. & Clin. Med. 42:801, 1953.
17. Kampmeier, R. H., and Smith, L. E.: Diffuse Arteritis as Recurrent Disease. Tr. Am. Clin. & Climatol. A. 65:232, 1955.
18. Clough, Paul W.: Editorial, Collagen Diseases, Ann. Int. Med. 42:209, 1955.

Discussion (Abstract)

Dr. A. Ford Wolf, Temple, Tex. Doctor Murphey has given us a comprehensive survey of the relation of allergy to the connective tissue diseases. It represents considerable work and a very complete review of the current literature. It was a difficult subject for anyone to cover and I think he did a splendid job of it. He is to be congratulated on his conservative stand and on his failure to get on the bandwagon of any of the more fanciful theories concerning the origin of the so-called collagen diseases.

I think we can at this stage conclude that the collagen diseases are extremely interesting; they represent a real challenge to investigative and diagnostic effort, and when we understand them, we will understand a great deal more of medicine and the body's physiopathologic response in general. I believe the consensus is that this group of diseases is an example of a physiopathologic change in one system of the body which may result from a variety of precipitating agents. We must postulate some underlying defect, possibly of a sensitivity nature. The mechanism is not understood, but the trigger factors may include tissue trauma, sensitivity processes, particularly drug and foreign protein allergy, infection, malignant disease, possibly psychosomatic upsets.

I can add nothing further regarding the causes of these diseases.

Paradoxic Gangrene Following Lumbar Sympathectomy

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The occasional complication of "paradoxic gangrene" following lumbar sympathectomy is not well understood. Several such instances are reported with the suggestion of an additional etiologic factor.

SYMPATHETIC GANGLIONECTOMY was first performed by Alexander of Liverpool in 1889 for epilepsy, and since then the operation has been used by many surgeons, with variable results, in the treatment of disorders of the circulation, many forms of pain, disturbances of the visceral motor mechanism, and in exophthalmic goiter, hypertension, hyperhidrosis, and bronchial asthma.

Lumbar sympathectomy has become an accepted procedure in the treatment of arteriosclerotic peripheral vascular disease. This relatively simple operation offers the best hope of arresting the progress of the disease. None of the many drugs or courses of medical treatment advocated for this condition has proved satisfactory. Sympathectomy in the earliest stages of the disease gives hope of improving the collateral circulation by producing vasodilatation in the vessels still capable of dilatation and of relieving the associated spasm in the involved and uninvolved vessels. Smithwick[1] has pointed out that in addition to improvement in the circulation to the skin and subcutaneous tissue, a more efficient muscular circulation may also occasionally be achieved, as judged by improvement in, or disappearance of intermittent claudication. This, he said, also applies to some patients with thromboangiitis obliterans.

Before recommending sympathectomy for patients having known organic disease, it is desirable to demonstrate by one method or another that the circulation can be improved. However, surgeons experienced in the treatment of peripheral vascular disease recognize that there is a small group of patients in whom preliminary tests indicate that operation will be ineffective, yet in whom sympathectomy has proved to be surprisingly worthwhile.

The over-all results following sympathectomy are good. Many extremities are salvaged and in some cases in which salvage is not possible the procedure enables the surgeon to amputate at a lower level with the assurance of healing at the amputation site. However, there is a dramatic complication which can occur following sympathectomy which, although fortunately rare, should be kept in mind. This is the development of acute gangrene immediately or soon after lumbar sympathectomy.

This complication remains incompletely understood although several theories have been proposed to explain it. Popoff,[2] in 1934, basing his theory on demonstrable anatomic grounds, attempted to explain the gangrene on the basis of arteriovenous shunts from the capillary system directly into the veins. According to this theory, following sympathectomy there occurs a general opening up of these small arteriovenous fistulae, further reducing the nutrient blood supply to the peripheral capillary bed. This explanation apparently has the most adherents. Cases have been reported by Atlas,[3] and by Freeman, Leeds and Gardner[4] in which the gangrene was attributed to the opening up of numerous arteriovenous communications.

Kleitsch and Kehne[5] recently reported a case of paradoxic gangrene following sympathectomy, and they suggested that factors other than arteriovenous shunts were responsible for the gangrene. It was their theory that the operation might precipitate a propagating thrombus by increasing the coagulability of the blood. Therefore, they advised the use of anticoagulant therapy preopera-

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tively and postoperatively in all cases considered for lumbar sympathectomy for arteriosclerosis. In our experience we have found anticoagulant therapy to be of doubtful value, and, in fact, the complications of therapy with the anticoagulants are so frequent that we have practically abandoned their use in thrombosis, embolism or any type of peripheral vascular disease. We feel that the anticoagulants are especially contraindicated in a patient considered for sympathectomy because of the danger of retroperitoneal hemorrhage occurring as a result of the dissection necessary at the time of surgery.

Woodhall[6] has reported two cases of so-called paradoxic gangrene and it was his feeling that gangrene occurring immediately after sympathectomy was commonly the result of the extent of the disease process present at the time of sympathectomy, or of the progression of vascular occlusion after sympathectomy. Woodhall mentioned White and Smithwick's "sensitization to adrenalin"[7] effect in extremities following sympathectomy in which color changes, sweating and coolness of the extremity occur. Edes[8] first noted this interesting phenomenon in the denervated ear of a rabbit. He noticed that if the animal became excited when chased or handled, the normal ear often equaled or surpassed in temperature the denervated one. Later, Smithwick, Freeman and White,[9] while investigating the failure of sympathectomy to relieve vasospasm in certain cases of Raynaud's disease, found that physiologic dilutions of epinephrine could produce intense vasoconstriction in the denervated arteries, and proved to their satisfaction that the adrenal gland can secrete sufficient amounts of adrenalin in response to cold, emotion, or insulin hypoglycemia to account for some of the failures of sympathetic denervation. They concluded that "restoration of tone in sympathectomized extremities is due in part to the sensitization of the neuro-effector mechanism to circulating hormones,—adrenalin and possibly a second sympathetic hormone, sympathin." Following this experimental work it was emphasized by White and Smithwick that operations on the sympathetic nervous system should be anatomically complete and sufficiently extensive to produce the minimum degree of sensitization and the maximum reduction in tone.

Among the theoretical causes for restoration of tone, Govaerts[10] has presented suggestive evidence that the peripheral sympathetic ganglion develops an independent activity after central connections have been cut. White and Smithwick[7] have obtained clear-cut evidence that decentralized human ganglia emit a striking outburst of impulses for a short period of time after preganglionic denervation. In addition, Cannon[11] thought that the maintenance of tone must result in part from an intrinsic property of smooth muscle itself, because muscle tone persists in the completely sympathectomized animal.

Kirtley, Garrett and Martin[12] have recently reported an evaluation of lumbar sympathectomy in 200 consecutive cases of peripheral vascular disorders. Four patients in this group developed "paradoxic" gangrene. These authors felt that the opening up of arteriovenous shunts might partly explain the gangrene, but in their opinion there was ample evidence that poor available collateral circulation and depression during the postoperative period were the main contributing factors.

Case Reports

We have recently seen three cases of gangrene occurring almost immediately after lumbar sympathectomy for arteriosclerotic peripheral vascular disease.

Case 1. J. L. H., a 65 year old man, was admitted to Touro Infirmary on January 3, 1953, with a history of gradually increasing pain in the left foot for two weeks. Four or five days before admission to the hospital, coldness and cyanosis of the foot and ankle had been noticed. These symptoms persisted and increased a little in severity until admission.

Past history was noncontributory with the exception of a chronic herpetiform dermatitis of the patient's entire body which had been treated for several years with little evidence of improvement.

Blood pressure on admission was 120/70. The positive findings on physical examination included generalized herpetiform dermatitis over the face, neck, trunk, and extremities, most marked over the back where several areas of secondary infection were present. The left foot was cold, and mottled areas of cyanosis extended proximally to about three inches above the ankle. Dorsalis pedis and posterior tibial arterial pulsations were not palpable. The leg from the knee to three inches above the ankle was warm and the popliteal and femoral pulsations were palpable.

On January 3 an emergency left lumbar sympathectomy was done under spinal anesthesia. The extremity was examined before the patient left the operating room and it was the opinion of the surgeon and his assistant that the foot appeared slightly more cyanotic than preoperatively. The temperature of the foot, determined by touch, showed no appreciable

change. The intern's note on the first postoperative day read "foot more cyanotic and colder." Within the next 72 hours there was a gradual progression of the cyanosis to frank gangrene of the first and second toes. The process then seemed to remain static with a tendency toward demarcation, so further observation was decided upon. The pain in the foot was only slightly less than before sympathectomy.

On January 17 a below-the-knee amputation (Maes type) was done under spinal anesthesia. There was minimal bleeding at this amputation and a tourniquet was not used. The stump was dressed on the first postoperative day and almost daily for the next ten days and it was soon evident that primary healing was not occurring. There was loss of an area of nonviable skin about 6 cm. in diameter at the lateral margin of the suture line. On February 1, 1953, a midthigh amputation (Maes type) was performed following which the patient had an uneventful recovery with primary healing. On the eighth postoperative day he was discharged from the hospital.

Case 2. W. A. P., a 72 year old man, was admitted to Touro Infirmary on March 17, 1951, with a history of intermittent claudication in the left leg of one year's duration. The condition had progressed to gangrene of the left fourth toe and, two weeks prior to admission to our service, a left lumbar sympathectomy had been done in another city. According to the patient's history the foot became worse immediately following sympathectomy.

On admission to Touro Infirmary the left foot was cold and cyanotic, and peripheral pulsations were absent. The left fourth toe was gangrenous with a cellulitis of the foot extending proximally.

On March 19, amputation (Maes type) below the knee was considered necessary. There was no healing at the amputation site, and on March 31 a midthigh amputation was done followed by primary healing. The patient was discharged on April 11, 1951.

Case 3. J. A. M., a 50 year old man, was admitted to the hospital on January 14, 1953, with the history of pain in the right foot of two months duration. The pain had been progressive and was intermittently accompanied by mild swelling of the dorsum of the foot. In addition the patient complained of pain in the calf of the leg after walking about one block.

Examination of the extremities revealed absent dorsalis pedis and posterior tibial arterial pulsations on the right. A faint posterior tibial arterial pulsation was palpable on the left. The foot was cold, became cyanotic when dependent, and blanched on elevation.

On January 15, 1953, a right lumbar sympathetic block was done with some decrease in pain and slightly increased tolerance to exercise. On January 19 a right lumbar sympathectomy was done. On the following day the patient complained of the foot being more painful and examination revealed increased edema of the dorsum of the foot. The foot was warmer than preoperatively but was still painful to palpation. On January 21, the foot was much more swollen and there was definite evidence of early ischemic gangrene of the toes, accompanied by cellulitis, and cyanosis of the dorsum of the foot. This condition progressed to a frank wet gangrene during the next 48 hours and on January 23, a below-the-knee amputation was done. The amputation site was dressed on January 29; the incision had healed primarily with no evidence of infection or ischemia. The patient was discharged from the hospital on February 2, 1953.

Discussion

These cases illustrate a complication of arteriosclerotic peripheral vascular disease which is, fortunately, rare but is serious when it does occur.

We feel that the gangrene which occasionally follows immediately after lumbar sympathectomy is probably due to a combination of the etiologic factors suggested by others in the rare patient who is unable to withstand such added trauma. Sometimes the optimistic surgeon hopes that sympathectomy will tip the scales in favor of preventing impending gangrene in a patient whose general condition and peripheral circulation are precarious. Unfortunately, the scales may occasionally be tipped the other way.

We would like to suggest one additional etiologic factor which may precipitate the sequence of events already outlined by Edes, Smithwick, and Cannon in such a patient. This factor is the mechanical one of the traction placed on the sympathetic chain during blunt and sharp dissection at lumbar sympathectomy. It is apparent that stimulation of the sympathetic chain occurs as a result of this traction and blunt dissection. It is possible that this stimulation first initiates vasoconstrictor activity in the peripheral smooth muscle of the vessels of the extremity and that muscle tone is then maintained for a sufficient length of time, after division of the sympathetic chain, to allow the smooth muscle to become sensitized to circulating sympathomimetic hormones. This process, in the presence of a less compromised circulation, probably results in only slight sensitization to circulating epinephrine and sympathin, and blood flow through the feet remains permanently increased. On the other hand this mechanism operating in a borderline case may provide the added burden which precipitates immediate gangrene. By the same reasoning, if we can agree with Cannon, the denervated arteriolar muscle may remain constricted long enough after traction stimulation for the muscle itself to manifest its so-called intrinsic property of maintaining tone.

Based on this theory we are now adding the simple procedure of injection of the sym-

pathetic chain and ganglia with 1 per cent Novocaine as soon as the chain is identified at operation. Thus, the chain and ganglia are temporarily anesthetized and are not sensitive to the stimulation caused by traction and dissection. We believe that the addition of this simple procedure may prevent the precipitation of gangrene in some patients with precariously poor circulation.

Whatever the etiology of "paradoxic gangrene," two practical considerations seem of importance in these patients. First, despite the fact that the arteriosclerotic peripheral vascular disease in some patients is so extensive that poor results can be anticipated, sympathectomy should be offered these patients because some extremities can still be salvaged. Gangrene is inevitable without operation, and its occurrence in an occasional case after operation should not deter us from offering patients this surgical treatment which appears at present to afford the best chance of delaying the progress of the disease and the appearance of its complications. It often happens, too, that even when the demonstrable improvement in the circulation and function of the limb appears trivial, the patient may obtain relief from the pain which had previously been troublesome.

The second point to bear in mind is that, since we know paradoxic gangrene does sometimes follow lumbar sympathectomy, bilateral simultaneous lumbar sympathectomies should not be considered in these cases. We believe this is an important consideration which has not been given enough attention in previously reported cases of "paradoxic gangrene."

Conclusions

1. "Paradoxic gangrene" does sometimes follow lumbar sympathectomy for arteriosclerosis.

2. Three cases of this condition have been reported from our own experience.

3. The various theories concerning the etiology of paradoxic gangrene have been mentioned and an additional theory of our own is suggested.

4. A simple surgical procedure is proposed as a means of possibly preventing the precipitation of gangrene in these patients undergoing sympathectomy for arteriosclerosis.

5. Lumbar sympathectomy should still be offered patients with arteriosclerosis, because it may delay the progress of the disease and the appearance of its complications.

6. Simultaneous bilateral sympathectomy for arteriosclerotic peripheral vascular disease should not be done.

References

1. Smithwick, R. H.: Surgery of the Autonomic Nervous System, New England J. Med. 240:543, 1949.
2. Popoff, N. W.: The Digital Vascular System, Arch. Path. 18:295, 1934.
3. Atlas, L. N.: Lumbar Sympathectomy in the Treatment of Peripheral Arteriosclerotic Disease, Am. Heart J. 23:493, 1942.
4. Freeman, N. E., Leeds, F. H., and Gardner, R. E.: Sympathectomy for Obliterative Arterial Disease; Indications and Contraindications, Ann. Surg. 126:873, 1927.
5. Kleitsch, W. P., and Kehne, J. W.: Paradoxic Gangrene following Lumbar Sympathectomy, Am. Heart J. 40:150, 1950.
6. Woodhall, J. P.: Gangrene Following Lumbar Sympathectomy for Arteriosclerotic Peripheral Vascular Disease, Surgery 32:1014, 1952.
7. White, J. C., and Smithwick, R. H.: The Autonomic Nervous System, New York, The Macmillan Company, 1944, pp. 174-175.
8. Edes, R. T.: The Physiology and Pathology of the Sympathetic or Ganglionic Nervous System, New York, William Woodard Co., 1869.
9. Smithwick, R. H., Freeman, N. E., and White, J. C.: Effect of Epinephrine on the Sympathectomized Human Extremity; An Additional Cause of Failure of Operations for Raynaud's Disease, Arch. Surg. 29:759, 1934.
10. Govaerts, J.: Quoted by White and Smithwick.[7]
11. Cannon, W. B.: Factors Affecting Vascular Tone, Am. Heart J. 14:383, 1937.
12. Kirtley, J. A., Garrett, S. Y., and Martin, R. S.: An Evaluation of Lumbar Sympathectomy in 200 Consecutive Cases of Peripheral Vascular Disorders, Surgery 33:256, 1953.

The Management of Paralytic Scoliosis*

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The author reviews several methods used in the surgical correction of scoliosis due to paralysis in children.

Source of Material

IN 1948, A SCOLIOSIS SERVICE WAS INITIATED at the Gillette State Hospital for Crippled Children in St. Paul, Minnesota. Since that time, 217 patients with scoliosis have been subjected to correction and fusion of their curve in this hospital. Sixty-five additional patients with scoliosis have been treated privately by the author in the same period and in a like manner.

Incidence of Paralytic Scoliosis

The reported incidence of paralytic scoliosis as compared to idiopathic, congenital and other types is subject to considerable variance. Cobb[1] indicated in 1948 that no more than 10 per cent of scoliosis was due to poliomyelitis, while 80 to 90 per cent of cases seen in a large scoliosis clinic were of the idiopathic type. It must be recognized that accurate statistical surveys are difficult. For example, I discovered only recently that no cross index file is maintained on outpatients at Gillette Hospital, and it is therefore possible to show the incidence of various types of scoliosis only in those patients admitted for fusion.

Since 1948, there were admitted to Gillette Hospital 99 patients with a diagnosis of paralytic curvature as compared to 79 with idiopathic and 33 with congenital scoliosis. The incidence of paralytic scoliosis in patients seen privately is approximately 50 per cent.

Conservative Treatment of Paralytic Curves

Conclusions reached in the conservative management of paralytic scoliosis can be discussed under several headings.

1. Every attempt must be made to overcome fascial contracture and muscle inequality prior to fusion. Iliotibial band contractures should have immediate surgical release because of their deforming influence on the spine and pelvis. Our experience with Lowman fascial transplants has been extensive enough to warrant the conclusion that progressive structural curves cannot be halted or controlled by this procedure alone. As an adjunct to other means of treatment of the curve, these transplants are of unquestioned benefit.

2. The release of contractures and the maintenance of flexibility of the spine is especially important in paralytic scoliosis in infants. Traction on the side on a convex frame has been found helpful in overcoming contractures above the pelvis. When flexible the spine is held comparatively straight in a Risser cast or Milwaukee brace. We have delayed fusion until the curve pattern becomes definitely established (Fig. 1).

3. High cervicothoracic curves should not be treated conservatively. Structural changes which are irreversible develop early in these curves, and a moderate degree of angulation is cosmetically deforming in this area. All such curves should therefore have immediate maximum correction and fusion.

4. There is a small group of patients with an early curve of a pattern which includes the area of approximately T7 to L2, which can be sometimes helped by wearing a high lift on the shoe and raising the pelvis on the convex side of the curve. A few such patients have been observed who have shown progressive improvement under such treatment throughout their growing years. There must be no obvious muscle imbalance in the trunk. Thoracic and low lumbar curves do not respond to this treatment (Fig. 2).

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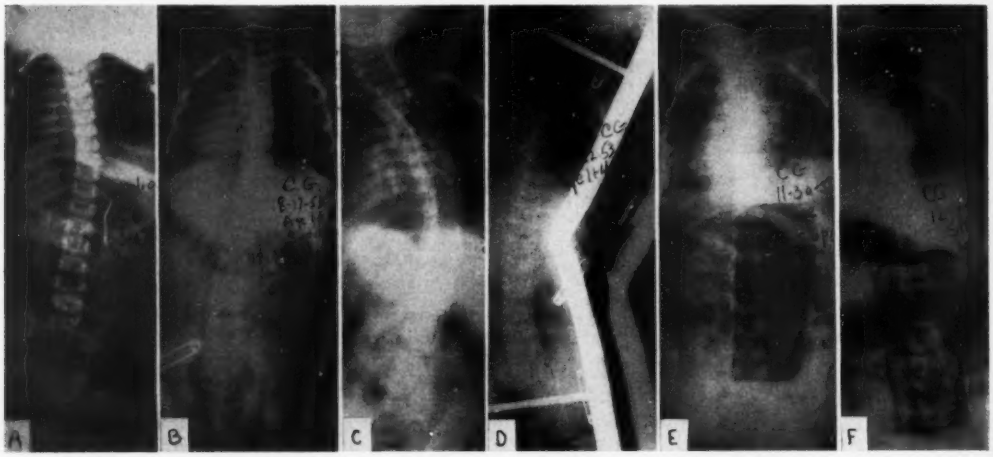
5. Attempts at holding a severe thoracic curve by a Risser cast or Milwaukee brace over a long period of time will result in progressive deformity of ribs and structural fixation of the curve. Such curvatures should be corrected and fused while they are still flexible, at whatever age they occur, for the cast or brace may help produce the "keel" deformity of the ribs.

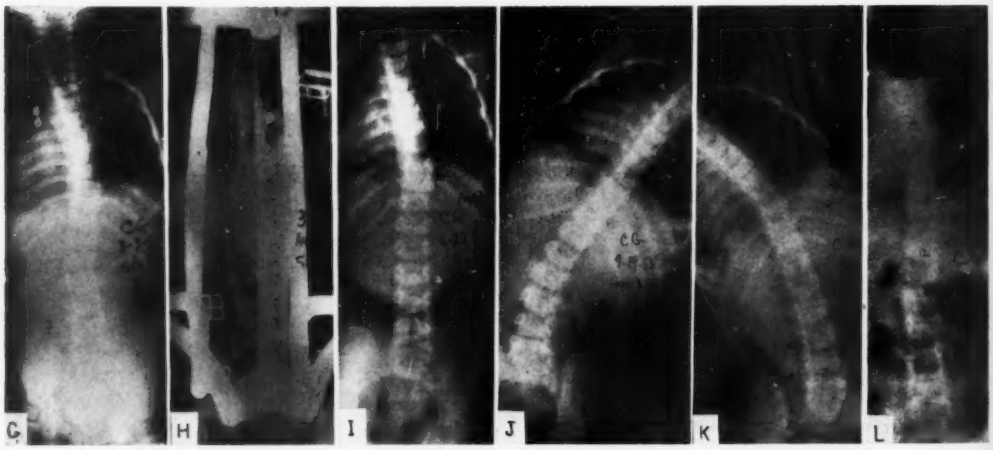
6. If a curve is to be treated by an external holding appliance, the choice lies among the Risser localizer cast, the Milwaukee brace, or the wedged (semibent) cast. There is no place for a corset or conventional body brace in the treatment of scoliosis. The Milwaukee brace is equally as efficient as the Risser cast, with the exception that the cast can be wedged to produce overcorrection of the

FIG. 1, A-F*



C. G. Polio age 4 months. (A) Age 10 months. Iliotibial band contracted on right; lateral abdominals absent on right, contracted on left. (B and C) Pelvic obliquity persisting after section of upper and lower ends right iliotibial band because of inequality above pelvic brim. Age 1 year, 3 months. (D) Stretching on convex frame to overcome tightness above pelvis on left. (E) Supine in Risser cast. Age 1 year, 6 months. (F) Standing in Risser cast. Age 1 year, 7 months.

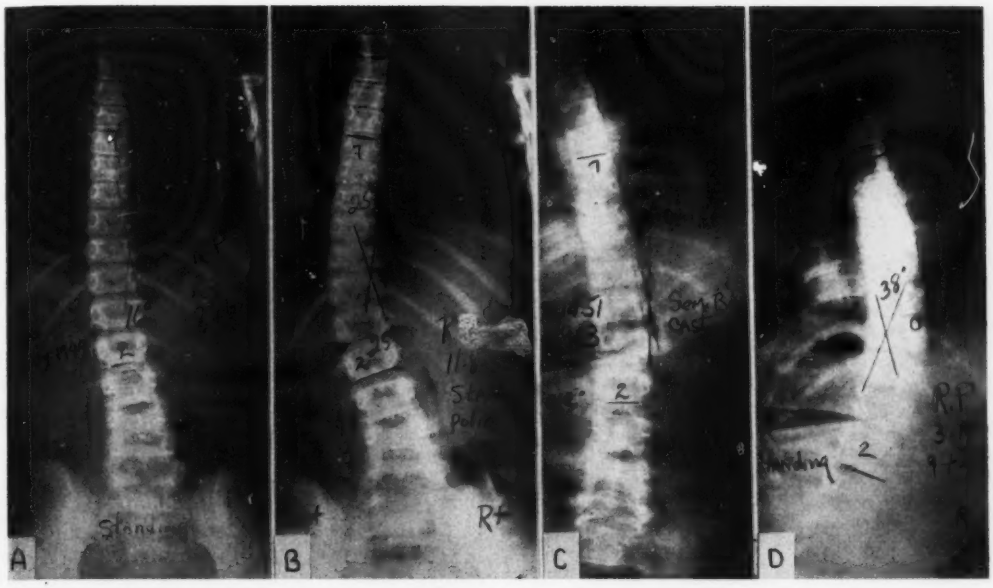
FIG. 1, G-L*



C. G. (G) Standing without external support. Age 1 year, 10 months. (H) Standing in Milwaukee brace. Age 1 year, 10 months. (I) Standing without external support. Age 3 years, 3 months. External support by Risser cast or Milwaukee brace has been continuous. Note persistence of pelvic obliquity due to unequal abdominal muscles. (J) Right bending film at age 3 years, 6 months. (K) Left bending film at same age. Lowman fascial transplant carried out 2 months prior on right side, anterior. (L) Risser cast correction is being continued.

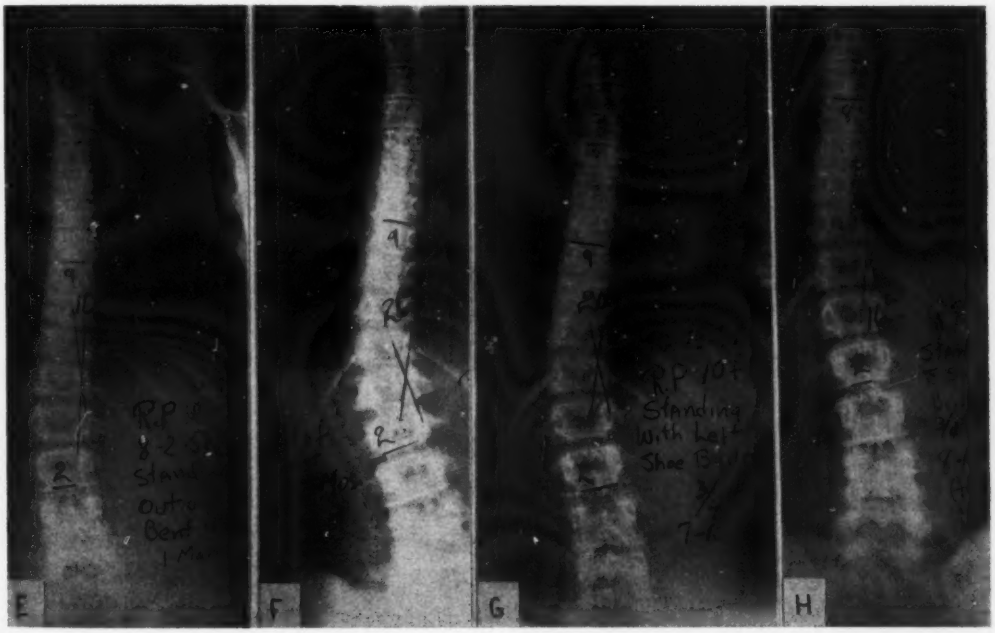
*All x-ray illustrations are shown as though the patient is viewed from the back, the right side of the x-ray representing the right side of the patient.

FIG. 2, A-D



R. P. (A and B) Progressive paralytic curve. No treatment. Legs are the same length. (C and D) Overcorrection of curve in semibent body cast.

FIG. 2, E-H



R. P. (E and F) Recurrence of same curve pattern after 5 months of overcorrection. (G and H) Gradual reduction of curve after building up shoe on convex side of curve.

FIG. 2, I-J

R. P. (I and J) Further reduction in curvature. Iliac apophyses now closing. Shoe lift can soon be discontinued.

curve, if that is desirable. We have felt that the resident training program on the scoliosis service should create complete familiarity with the Risser localizer cast, and also with the Milwaukee brace. The resident staff should also know the value of the semibent body cast in certain low curves, and that resistant structural curves can often best be loosened by means of the hinged turnbuckle cast.

The Role of the Iliotibial Band in the Production of Scoliosis

Unilateral or bilateral contractures of the iliotibial band are commonly seen in poliomyelitis. When bilateral, the amount of contracture may be unequal and the more severely contracted side may hide the opposite contracture. In such an event surgical release of the tightest side may be followed by reversal of the pelvic obliquity.

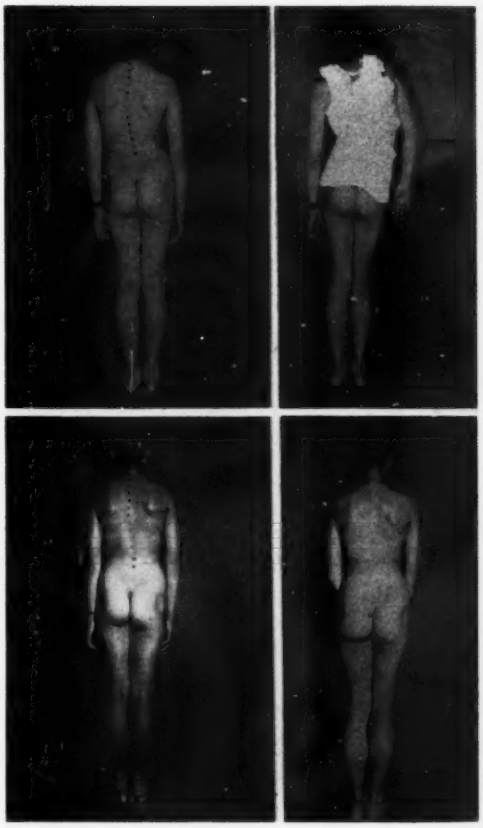
In the presence of trunk paralysis, without contracture above the pelvis, a severe scoliosis may accompany contracture below the pelvis. In time, such a curvature will become structural, but in its earlier years it will be relatively flexible, and can be adequately corrected and held by fusion after the iliotibial band contracture has been released (Fig. 3).

No discussion of the contracted iliotibial band should be presented without acknowledgement of credit and honor to the work of Yount[2] and Irwin.[3] The role of the iliotibial band in producing structural deformities of the pelvis and spine was insufficiently recognized until Irwin's classic description in 1949 of the deformities produced by this contracture and of the efficient treatment which can be given.

Contractures Above the Pelvic Brim

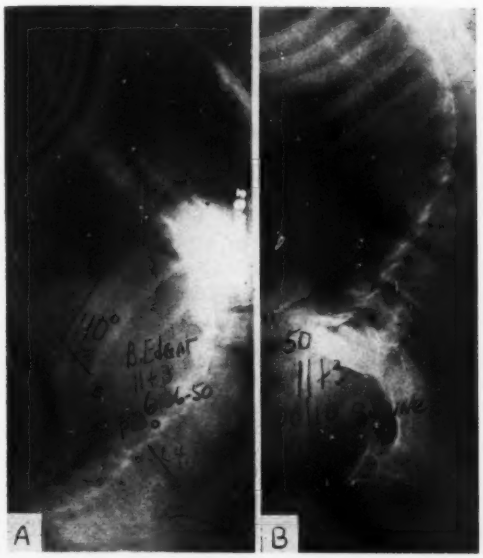
When there exists a combination of lateral overpull above the pelvis with iliotibial band contracture below on the opposite side, the stage is set for a severe scoliosis. Release of contractures below, followed by correction with a cast and adequate fusion of the curve, should be combined with Lowman fascial

FIG. 2, K



R. P. Patient's appearance during the 5 year period of observation.

FIG. 3, A-B



B. E. (A and B) Severe paralytic curve with marked iliotibial band contracture; 70° hip flexion contracture was present.

transplants and erector spinae transplants. In the young patient the continued presence of contracture or muscle overpull may cause the plastic living graft to slowly bend during the growth period. This has very rarely occurred in our experience without the aid of an unrecognized pseudoarthrosis or a fusion of inadequate length. External protection of the fused curve may help prevent loss of correction, and should be continued for a long period of time in the young patient where muscle inequality of severe degree persists.

Selection of the Patient for Fusion

Much controversy has prevailed concerning the dire consequences which follow correction and fusion of a curve in the young child. In our experience, the age limit for fusions has been safely dropping. Lessons learned in fusing the young patient include the following:

1. Long fusions, usually from parallel to parallel vertebrae, are safest.

2. Disaster will follow if curves are fused short and if the fusion is not properly extended as the spine begins to bend above and below the fusion area.

3. The presence of a pseudoarthrosis in the unprotected fusion area will result in a severe loss of correction. Due to growth changes recorrection often becomes quite impossible.

Risser's wide experience in fusion of curves in the young child leads him to the belief that loss of correction to an appreciable amount can be avoided if the above rules are followed. He does not feel that fusion in the young will produce a lordosis, but points out that if a spine is fused in lordosis the deformity will persist.

My experience covers several years of observation of paralytic curves fused at age 9 to 11 and older. It is only in the last two years that patients younger than this have been fused. I have not observed the development of a recurvatum deformity, and loss of correction has occurred only for a good reason (Fig. 4).

One can expect that most curvatures from poliomyelitis will progress and become deforming. In the absence of obvious muscle inequality in the trunk, conservative treat-

FIG. 3, C-D

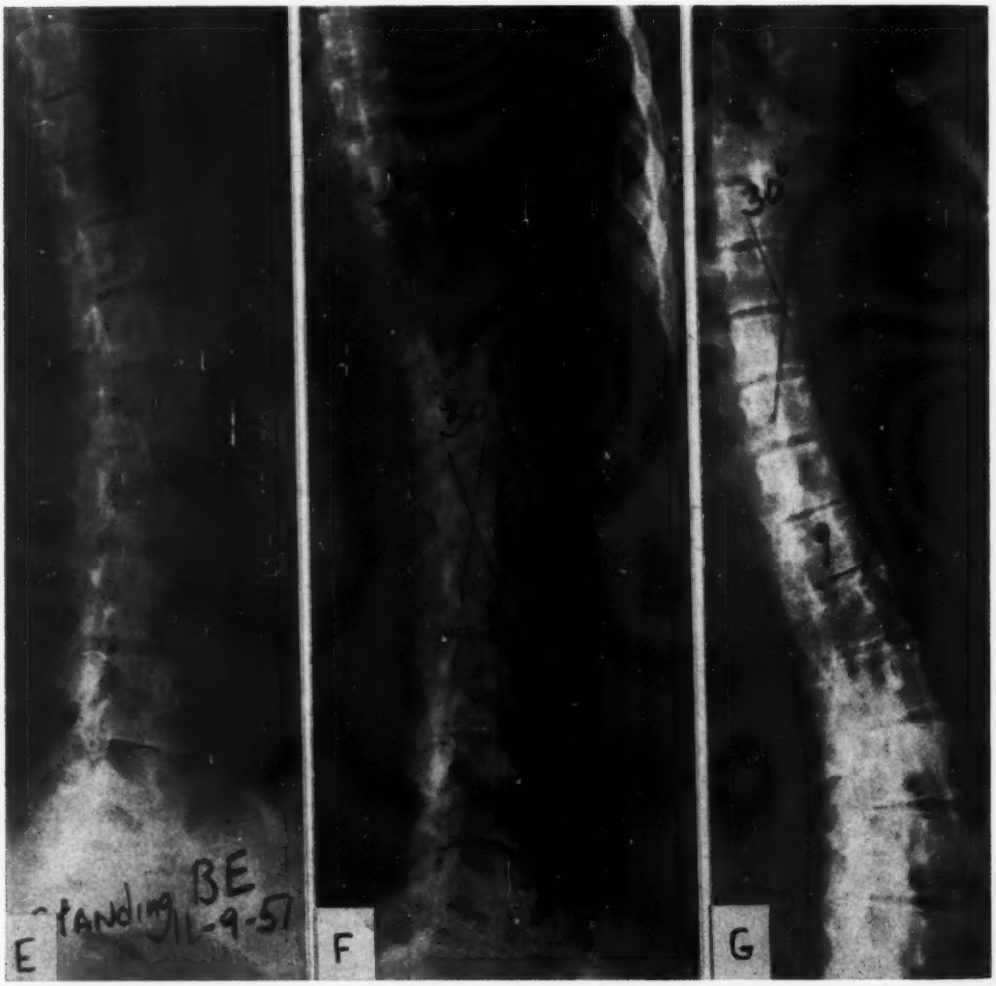
B. E. (C) After complete release of contractures below the pelvic brim and postoperative stretching, the curve was corrected in a wedging cast which included both legs. (D) Six months after fusion the cast was changed to leave the legs free.

ment should be carried out in the early curve until progression is noted. Risser's iliac apophysis sign of spinal growth termination is not as important in curves due to poliomyelitis as it is in idiopathic curves, for paralytic scoliosis may progress after spinal growth has ceased.

Methods of Correction

During the early years of experience, the hinged turnbuckle cast was used for the most part, applied as suggested by Cobb,[4] with the patient first bent to correct the compensatory curves. The Milwaukee brace was also used frequently, usually very successfully, but erratic fitting by the brace shop made its use somewhat discouraging. With the advent of the present Risser frame, the Risser localizer cast[5] has been used most frequently. We discovered long ago that a freshly applied cast can be immediately wedged, using the plaster as hinges. We have found such rapid correction to be just as efficient in the average curve as was the slow correction by the turn-

FIG. 3, E-G



B. E. (E) One year after fusion the graft was solid and correction was maintained without external support. (F and G) Five years after fusion the correction is maintained. Note that the fusion included only D8 to L3. The rotation continues to L5. It is not necessary to carry the fusion across the sacrum in low lumbar curves except rarely. If the curve above D9 had been structural it would have been necessary to include it in the fusion area.

buckle. Curves which are very rigid must often be corrected slowly.

Maintenance of Correction

We have not found it possible to always maintain the maximum correction which is obtained. Risser's masterful application of a skin tight cast with scarcely any padding allows ambulation in his patients at once without loss of correction. In my experience, a comparison of the supine x-ray film taken just after the cast has been applied, with another taken standing at a later time, will almost invariably show a loss of correction of from 10 to 25 degrees. The loss of correction is sometimes mildly progressive with continued ambulation. It is more marked in low curves and in curves which are only partially correctible. Patients with curves which can be very nearly straightened can be allowed up in a Risser localized cast without appreciable loss of correction. There is often a little gradual loss even though the patient is kept supine throughout the course of treatment, but this is seldom more than a few degrees.

We have used vigorous correction in the preoperative cast and have kept the patient supine thereafter. This is probably the reason why our attempts to obtain more correction postoperatively by change of cast have met with failure. Risser,[6] Schmidt[7] and Blount[8] all feel that the spine is considerably loosened by the fusion and is therefore more easily correctible.

Determination of the Fusion Area

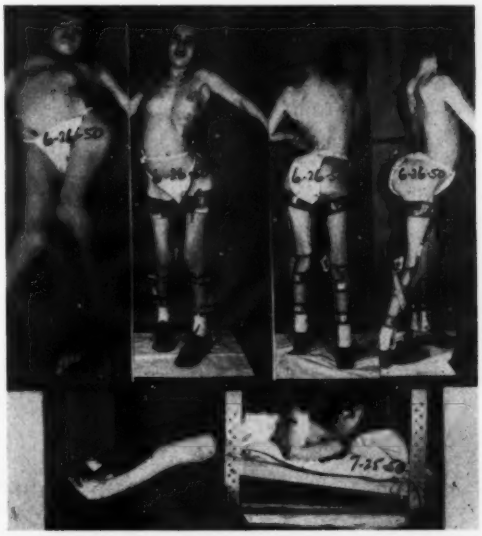
The teachings of Cobb,[1,4,9,10] Risser,[5,6,11] Schmidt[7,12] and Blount[8] have been freely drawn upon in presenting the following discussion. Much is taken directly from Schmidt's[12] article outlining the fundamental principles of treatment of scoliosis.

The ends of the primary curve are determined by three criteria. They are:

1. Vertebral interspace wedging becoming neutral or reversed,
2. Vertebral body tipping becoming maximal, and
3. Neutral rotation being present.

In many curves all three of these criteria are satisfied at the same level. If so, the primary curve to be measured will coincide with the fusion area.

FIG. 3, H



B. E. Photographs of patient before treatment. The lower picture shows patient being stretched after bilateral release of contractures and before the scoliosis was treated.

In many idiopathic curves of the common right thoracic pattern, and in an occasional paralytic curve, all three criteria are found satisfied at the same level and the fusion then needs only to include the full extent of the primary curve, or at the most, an additional vertebra below.

There are thoracolumbar curves found in both idiopathic and paralytic types in which Criteria 1 and 2 are satisfied at one level while rotation toward the convexity of the primary curve continues below for one, two, or three vertebrae. In such cases the measured curve is determined by satisfaction of Criteria 1 and 2, while the fusion area must be ex-

FIG. 3, I

B. E. The postoperative result. Correction is being maintained in 1955 as in 1953.

tended to include the neutral end vertebra (Fig. 5).

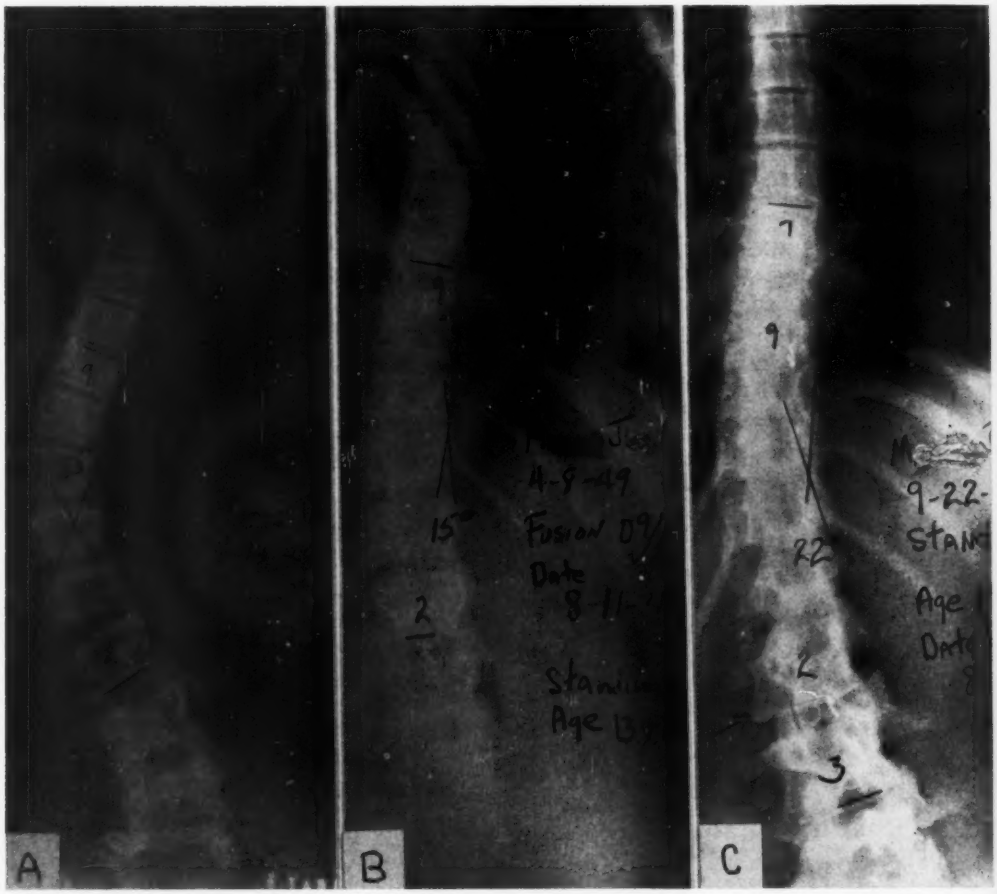
Low lumbar curves will often demonstrate satisfaction of Criteria 1 and 2 at the fourth interspace, with rotation continuing into the fifth lumbar vertebra. Here, it is *not* necessary to extend the fusion to the sacrum. Correction will be satisfactorily maintained if the fusion includes the lowest vertebra which satisfies Criteria 1 and 2 (Fig. 6).

It is very seldom desirable to extend the fusion on to the sacrum. One exception is the permanent wheel chair patient with a flail trunk whose sacrum and pelvis are oblique and form a continuation of the lumbar curve.

An upper thoracic primary curve is sometimes found with no structural curve of the spine below. One should fuse these curves from parallel to parallel vertebrae in the young with the curves well corrected. In some older, severely structural curves, it is necessary to extend the fusion well beyond the ends of the curve.

An upper thoracic curve may be found in conjunction with a thoracic-lumbar curve below, both of which will be structural. In such a pattern, both curves will be included in the

FIG. 4, A-C



M. J. (A) Post-polio left curve D5 to L2, 55° standing. Age 12 plus 1. Note that D8 and L3 are the neutral end vertebrae and should have been included in the fusion area. (B) Fusion D9 to L2; 8 months postoperative. Correction now at 15°. Maximum correction was at 10°. (C) Five years later. The curve has lengthened to include D7 and L3 and has increased somewhat.

fusion area. This usually means fusion from parallel to parallel vertebrae (Fig. 7).

A thoracolumbar curve may be found extending from about D8 or D9, to L3 or L4, with the compensatory curve above being functional as determined by side bending films. Here the curve need not be fused throughout the dorsal curve area, but only one or two vertebrae into it, especially in the older group. The curve above must be watched closely in the young growing spine, for it may progress even though not initially structural.

Long thoracolumbar curves are found where the upper limit of the curve is indefinite as determined by interspace wedging, rotation, and tilting. In such curves, the fusion is carried into the upper thoracic spine, frequently to the first thoracic vertebra, especially in the young patient (Fig. 8).

Double curves, with the junction between them at the region of D12 are not uncommon in poliomyelitis. Both are structural and progressive, and both curves must be fully fused. The occurrence of pseudoarthroses has plagued our efforts in many of these.

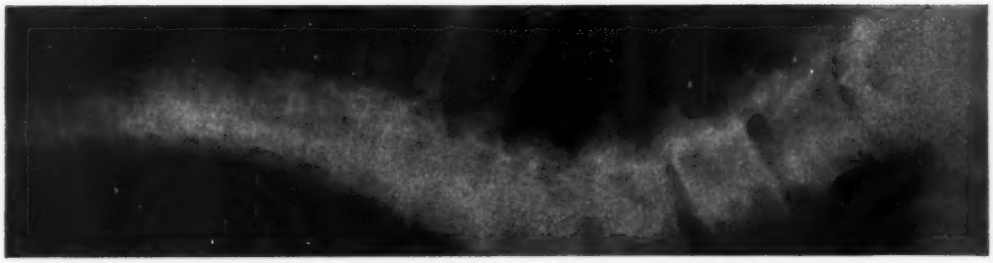
FIG. 4, D

M. J. The end result still remains satisfactory in spite of a fusion area which is too short.

FIG. 5, A-B

(A) The position of the pedicles in relation to the vertebral bodies determines the amount of rotation present more accurately than does the position of the spinous process. In this x-ray D6 and L2 show maximal tilt. D5-6 and L2-3 show reversal of interspace wedging. Rotation continues below through L3, and L4 is the first completely neutral vertebra. D5 is neutral above. Based on this film the measured curve is D6-L2 while the fusion area planned should be D5-L4. (B) The correction film must also be considered. L2 is now neutral and L3 has opposite rotation. With this amount of correction, it is safe to fuse D5-L3.

FIG. 6



A low lumbar paralytic curve. The measured curve indicated by maximal tilt and neutral interspace is D11 to L4. Rotation is from neutral vertebrae D9 to L5. Fusion area is D9 to L4.

Technic of Fusion

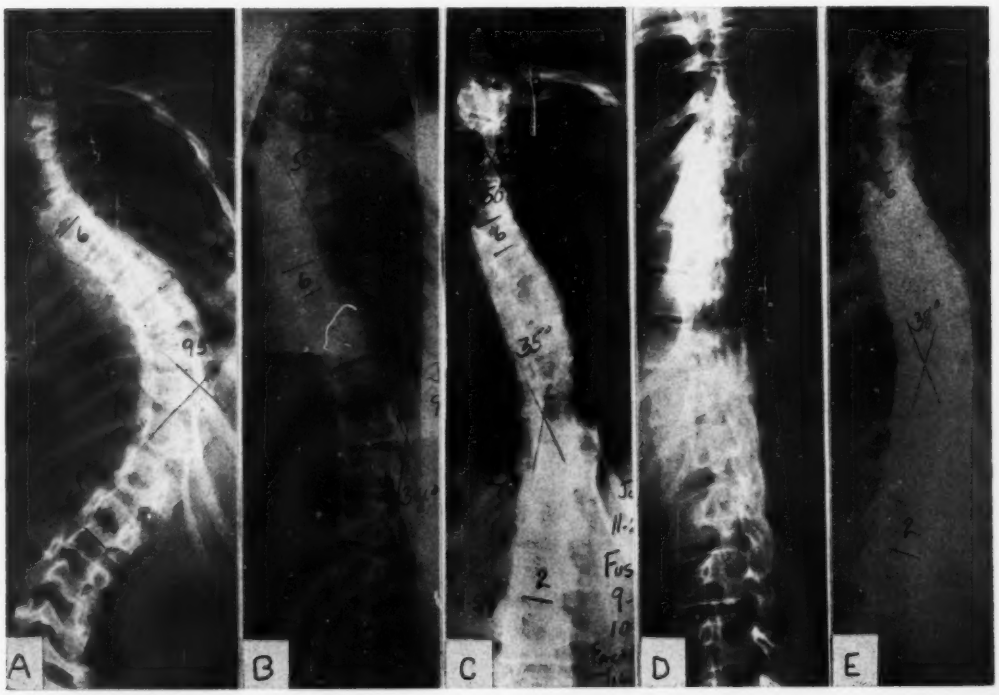
It is quite certain that most surgeons of experience in spinal fusions devise modifications in technic which they like to call their own. In doing a facet fusion, little improvement over the original technic used by Hibbs can be devised.

The fusion is done through a windowed cast. It is possible to cut the cast widely over the iliac crests posteriorly so that bone from the ilium can be obtained.

The incision is made as straight as possible for Cobb[4] has pointed out that a straight incision makes the spine look straighter.

Meticulous removal of soft tissue is carried out to the tips of the transverse processes in the dorsal spine and beyond the facets in the lumbar spine. The facets in both areas must

FIG. 7, A-E



J. Z. (A) Post-polio curve; D6 to L2, 95°. Age 11 plus 7. Fusion area should be D1 to L3. (B) Upper compensatory curve does not straighten as well in Risser cast as it did on side bending. Lower curve straightens well. (C) Fusion area D1 to L3. One year postoperative. Facet fusion and tibial bone. (D) Oblique view shows graft solid at one year. (E) Correction is maintained 2 years postoperative.

be completely cleared of ligamentous tissue using a curette and a small ethmoid (pituitary) rongeur. In the lumbar spine the facets are thoroughly curetted with a very small and very sharp curette, after which the opposing bony surfaces of the facet are crushed by the technic of Chandler or Risser. Thick leaves of bone are turned down in a criss-cross from the spines and laminae adjacent (Fig. 9). Recently, this technic has been changed in favor of insertion of blocks of iliac bone into facets which have been thoroughly excised, countersinking the caudal end of the block into a prepared bed in the pars interarticularis.

In the thoracic spine a leaf of bone is raised over the facet, giving direct access to the facet surface from which nearly all cartilage is removed. A rim is left adjacent to the dura. A substantial piece of bone is then turned down from the nearby transverse process, leaving it attached if possible, and impacting its tip directly into the cleaned out facet area. Multiple leaves of bone, as thick as possible, are then turned down in a criss-cross manner, tucking their ends into appropriately placed trap doors of bone. A substantial bed of bone is added from the ilium or tibia to the lumbar and lower dorsal fusion area and to the upper dorsal area if plenty of bone is available (Fig. 10).

Occurrence of Pseudoarthrosis

The fusions in this series of 128 paralytic scolioses have been performed for the most part by the senior residents at the Gillette Hospital. About one-fourth of the fusions have been done by me, the rest by the residents under part-time supervision by the author. The statistical results presented do, therefore, represent a cross section of the work done by orthopedic surgeons of average ability. Each resident has had the technic demonstrated to him adequately. No startling difference has been observed in the results of fusions performed by the resident group and those done by me.

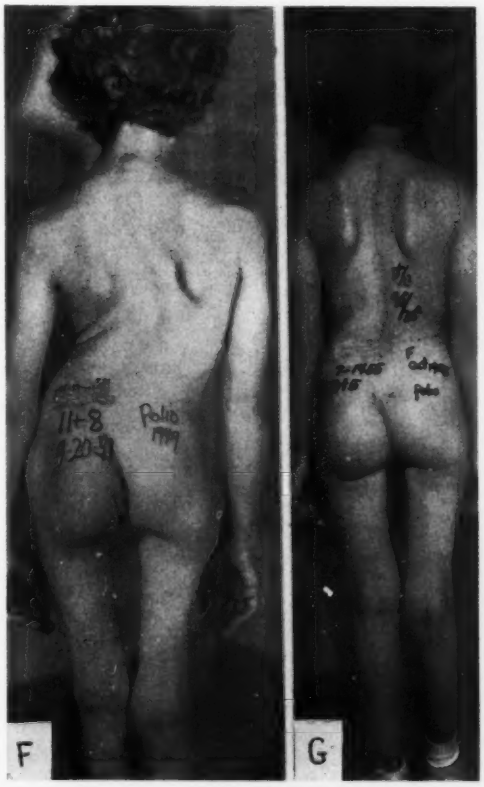
Four types of fusions have been performed.

Group I. Initially, during 1948-50, the method of fusion consisted of rough stripping of spinous processes and laminae by sharp osteotome dissection. There was no attempt at meticulous soft tissue removal. The laminae were chipped up and roughened. The spinous processes were turned down in strips. The joints were not exposed and the transverse processes in the dorsal area were not exposed. Bone was added in the form of reed grafts, struts, or crumbled bone.

Group II. During the years 1950-52, the method of fusion followed as closely as possible that used by Cobb.[4] This consisted of meticulous subperiosteal soft tissue removal from spinous processes, laminae, lumbar mamillary processes and dorsal transverse processes. Attached flaps of bone were raised and locked under small trapdoors of bone raised on adjacent vertebral surfaces. All available local bone was utilized in this manner. Bone from another source was added in large amounts. The joints were not disturbed.

Group III, Group IV. Since 1953, facet fusions have been done. This technic has already been described. In Group III, no bone from another source was added, while in

FIG. 7, F-G



J. Z. (F and G) Pre- and post-correction photographs.

Group IV, autogenous or bank bone was added to the facet fusion.

Statistical survey discloses the following information.

Group I. There were 49 paralytic curves in this group. Autogenous bone was added in 33, of which 64 per cent developed pseudoarthroses. Bank bone added in 5 gave 40 per cent and in another 5 in which deficient autogenous bone was reinforced by bank bone there were 80 per cent of pseudoarthroses. There were 6 patients in whom the type of bone used was not recorded. Fifty per cent of these developed a defect in the graft. In the total group there were 61.5 per cent of pseudoarthroses (Table 1).

Group II. There were 34 paralytic curves in this group. Autogenous bone added in 17 patients gave only 18 per cent of pseudoarthroses. Bank bone in 6 gave 84 per cent, while in 2 others, bank bone plus autogenous bone showed a defect developing in one. Nine patients with no record of the type of bone added showed a pseudoarthrosis in 50 per cent. The whole group of 34 patients showed a graft defect in 44 per cent (Table 2).

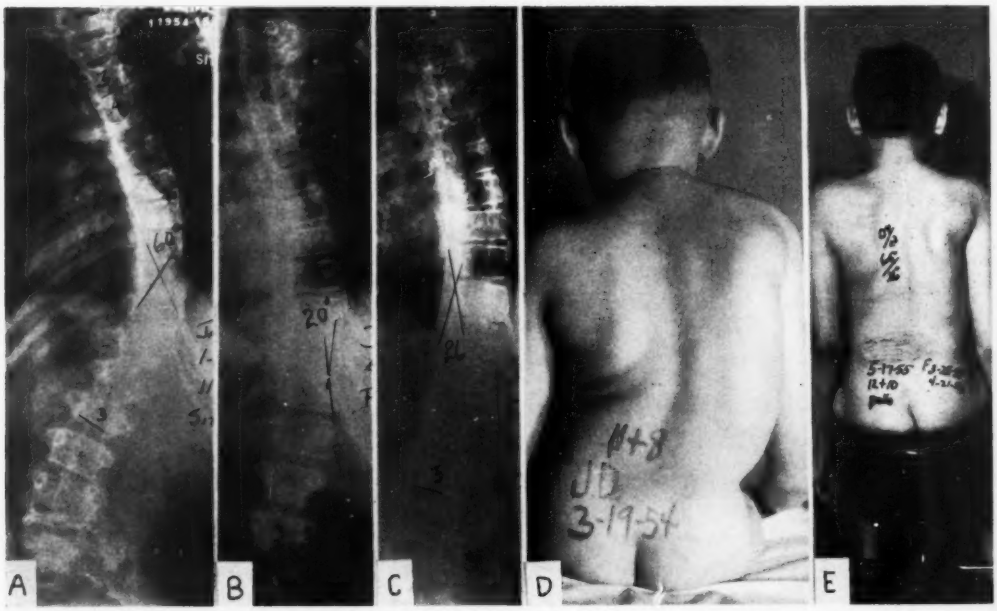
TABLE 1

Group I (Early Fusions)	
Autogenous Bone Added	Total=33
Fusions	12 (36%)
Pseudoarthroses	21 (64%)
Bone Bank Bone Added	Total=5
Fusions	3 (60%)
Pseudoarthroses	2 (40%)
Bone Bank Bone Plus Autogenous	Total=5
Fusions	1 (20%)
Pseudoarthroses	4 (80%)
Type Bone Added Not Recorded	Total=6
Fusions	3 (50%)
Pseudoarthroses	3 (50%)
Total Patients Group I—49	
Fusions	19 (38.5%)
Pseudoarthroses	30 (61.5%)

Group III. There were 24 patients with facet fusions with no additional bone added. Forty-six per cent of these developed a pseudoarthrosis.

Group IV. There were 21 patients analyzed. In 9, autogenous bone added to the facet fusion resulted in solid fusion in all. In 10, bank bone added gave 30 per cent pseudoarthrosis. In 3 additional patients,

FIG. 8, A-E



J. D. (A) Polio curve D3 (D4) to L3. Fusion area should be D2 to L4. Jan. 1954 age 11 plus 8; 60° sitting. (B) Correction at 20°. Fusion went only to L3. Note that L3 is now neutral. Facet fusion without bone added. Fusion March and April 1954 D1 to L3. (C) Correction nearly maintained. Out of plaster 4 months, without loss. Further loss is not expected in spite of slightly inadequate fusion area. At 18 months post-fusion, correction remains the same (May 17, 1955). Sitting 26°. (D and E) Pre- and post-correction photographs.

TABLE 2

Group II (Cobb Fusions)		
Autogenous Bone Added	Total=17	
Fusions	14	(82%)
Pseudoarthroses	3	(18%)
Bone Bank Bone Added	Total=6	
Fusions	1	(16%)
Pseudoarthroses	5	(84%)
Bone Bank Bone Plus Autogenous	Total=2	
Fusions	1	(50%)
Pseudoarthroses	1	(50%)
Type Bone Added Not Recorded	Total=9	
Fusions	3	(33%)
Pseudoarthroses	6	(66%)
Total Patients Group II—34		
Fusions	19	(56%)
Pseudoarthroses	15	(44%)

TABLE 3

Group III Facet Fusions—No Bone Added		
Total Number Checked	24	
Fusions	13	(54%)
Pseudoarthroses	11	(46%)
Group IV Facet Fusions With Bone Added		
Total Number Checked	21	
Facet Fusion Plus Autogenous Bone	9	
Fusions	9	(100%)
Pseudoarthroses	0	
Facet Fusion Plus Bone Bank Bone	10	
Fusions	7	(70%)
Pseudoarthroses	3	(30%)
Facet Fusion With Bone Added Type of Bone Not Recorded	3	
Fusions	2	(66%)
Pseudoarthroses	1	(33%)

there was no record of the type of bone added. In one of these there was a pseudoarthrosis (Table 3).

Based on this analysis, certain impressions become evident.

1. Fusions done with indifferent exposure result in a high percentage of pseudoarthrosis even if autogenous bone is added.

2. Meticulous wide exposure, with removal of all soft tissue and careful interlocking of bone flaps (Cobb technic) results in a satisfactory percentage of solid fusions, provided that autogenous bone is used.

3. Autogenous bone is superior to bank bone as graft material.

4. Facet fusions without addition of bone from another source result in an unsatisfactory percentage of fusions.

5. Facet fusions with autogenous bone added result in solid fusion in a high percentage of patients.

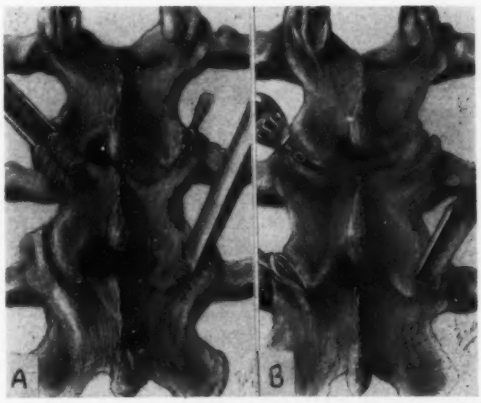
Location of the Pseudoarthrosis

The largest number of pseudoarthroses were found between D11 and D12 and between D12 and L1. The reasons for this are speculative, but may include the fact that the structure of the vertebrae in this transitional area is such that it is difficult to create good interlocking bone flaps and to destroy and close the facets. It is also likely that a longer and more flexible curve offers greater opportunity for defects to develop because of increased movement. Our experience points clearly to the fact that idiopathic dorsal curves of the D5 to D12 pattern fuse more readily than do the longer curves (Fig. 11).

Treatment of Pseudoarthroses

Loss of correction from the presence of a pseudoarthrosis need not occur if the presence of the defect is recognized, properly protected, and treated by exploration and refusion. A problem in my experience has been the hypnotic-like state of mind which can arise in the orthopedic surgeon, where, out of sympathy for the patient's desire to have the cast removed, a questionable graft is allowed to go unprotected and unexplored. At each interval follow-up examination a slight loss of correction is noted. It is not until considerable time has elapsed that the sum total of these continual small losses is finally recognized as a major and sometimes total loss of correction. By this time, recorrection and refusion may

FIG. 9, A-B



(A) Risser technic of fusion of the lumbar facets. (B) Chandler technic of fusion of lumbar facets.

FIG. 10, A-B

(A) Showing a method of fusion of dorsal spine used by the author. The facets are exposed by raising leaf of bone and are thoroughly scraped. A large leaf of bone is turned into the demolished facet from the transverse process of the vertebra below. (B) Criss-crossing leaves of bone are turned from the spinous processes and laminae.

be difficult or impossible, and the tolerance of patients and parent toward further treatment may have reached an end.

Early recognition of defects in the graft is therefore essential. Careful study of the entire graft by anteroposterior and two oblique views are made 6 months after fusion. Suspicious areas are watched for an additional 2 months, at which time exploration should be carried out on all persisting defects. Refusion of the defect is a short and relatively minor procedure. The patient need not as a rule remain supine beyond the time he would normally become ambulatory. In many of the lower curves a snug body cast is the only external protection needed. The occurrence of a pseudoarthrosis need not, therefore, be a dreaded experience for the patient.

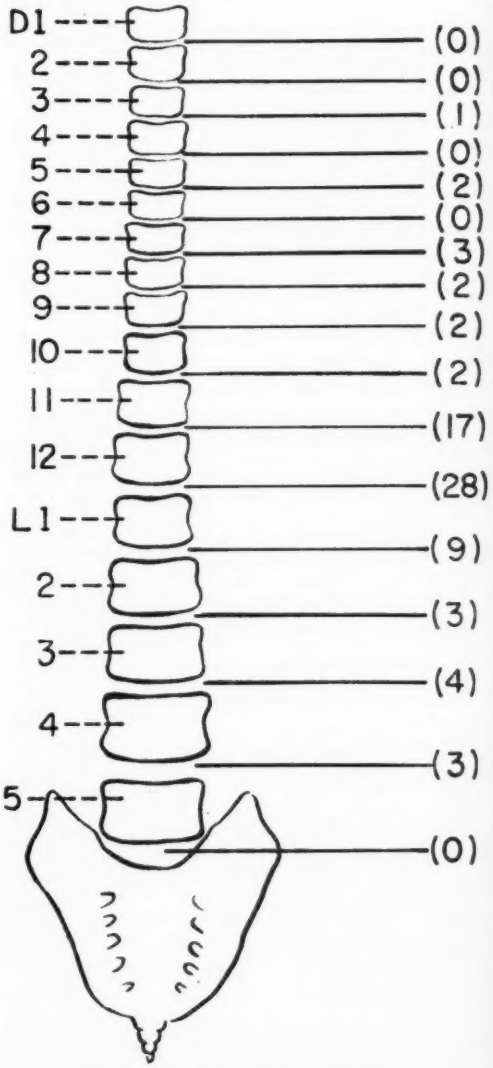
Fracture of the Graft

Fracture of the graft has occurred only once in this series. This patient was solidly fused at 11 months and her cast was removed. Shortly thereafter she was involved in a carbicycle collision. Loss of correction followed and a large defect in the graft was apparent. Recorrection and refusion were easily accomplished with the patient remaining ambulatory in a body cast.

Delayed Appearance of a Pseudoarthrosis

Delayed appearance of the pseudoarthrosis has been reported. With one possible exception, we have not seen this happen. In this patient, fused by the Cobb technic with a large tibial strut placed on one side, the strut remained intact and became viable as shown by x-ray appearance. A defect then became evident in the strut several months after the cast was removed. On re-examining the x-ray films, it is noted that the graft area opposite the strut was inadequate at the spot where the defect appeared. It was felt that the strut was subjected to excessive strain at this point

FIG. 11



Incidence of location of pseudoarthroses.

and that a fatigue fracture occurred. The pseudoarthrosis became completely solid subsequently, without specific treatment, but there was considerable loss of correction.

Causes of Loss of Correction in Scoliosis

In summary, the failures in scoliosis are for the most part attributable to errors in judgment by the orthopedic surgeon in charge. These causes for failure are:

1. The presence of one or more pseudoarthroses in the fusion area.
2. Inadequate length of the fusion area.
3. Failure to correct severe soft tissue contracture prior to correction and fusion of the curve.
4. Failure to correct severe lateral or abdominal muscle imbalance before or soon after correction and fusion of the curve in young paralytic scoliosis patients.
5. Inadequate external support of the corrected curve for a sufficient time to insure a mature and solid bony fusion.

Conclusions

The results of study of 128 paralytic curves corrected and fused by four different technics are presented. This is a preliminary report because analysis of these patients, and other patients now under treatment, is continuing. The occurrence of pseudoarthroses in the graft has been and remains the main obstacle toward consistently good results in the treatment of scoliosis. Results of this study show that the highest percentage of solid fusions occurred in patients who had facet fusions with autogenous bone added and in those who had the Cobb method of fusion with autogenous bone added.

Loss of correction from the development of a defect in the graft need not occur provided that the defect is recognized in time and properly treated.

Inadequate length of the fusion area is the second most common cause of loss of correction.

No ill effects have been observed in this series from fusions done in the age group above 8 years, except in those in whom the fusion was inadequate in length or a pseudoarthrosis developed.

References

1. Cobb, J. R.: Outline for the Study of Scoliosis, Am. Acad. Orthopedic Surgeons, Instructional Course Lectures, 5:261, Ann Arbor, J. W. Edwards, 1948.
2. Yount, C. C.: The Role of the Tensor Fascia Femoris in Certain Deformities of the Lower Extremities, J. Bone & Joint Surg. 8:171, 1926.
3. Irwin, C. E.: The Iliotibial Band, Its Role in Producing Deformity in Poliomyelitis, J. Bone & Joint Surg. 31-A: 141, 1949.
4. Cobb, J. R.: Technique, After-Treatment, and Results of Spinal Fusion for Scoliosis, Am. Acad. Orthopedic Surgeons, Instructional Course Lectures, 9:65, Ann Arbor, J. W. Edwards, 1952.
5. Risser, J. C., Lauder, C. H., Norquist, D. N., and Craig, W. A.: Three Types of Body Casts, Am. Acad. Orthopedic Surgeons, Instructional Course Lectures, 10:131, Ann Arbor, J. W. Edwards, 1953.
6. Risser, J. C.: Personal communication.
7. Schmidt, A. C.: Personal communication.
8. Blount, W. P.: Personal communication.
9. Cobb, J. R.: Correction of Scoliosis in Poliomyelitis. Second International Poliomyelitis Conference, Philadelphia, J. B. Lippincott Co., 1952.
10. Cobb, J. R.: Personal communication.
11. Risser, J. C.: Important Practical Facts in the Treatment of Scoliosis, Am. Acad. Orthopedic Surgeons, Instructional Course Lectures, 5:248, Ann Arbor, J. W. Edwards, 1948.
12. Schmidt, A. C.: Principles in the Treatment of Scoliosis, Sonderabdruck aus Verhandlungen der Deutchen Orthopadischen Gesellschaft, 41, Kongress, Munster.

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The Ocular Manifestations of the Sturge-Weber Syndrome*

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The author considers the ocular lesions of this syndrome as they may occur without overt meningeal lesions. He describes a diagnostic maneuver which may differentiate hemangiomas of the choroid from malignant melanomas if glaucoma has not developed.

THE STURGE-WEBER SYNDROME, or encephalotrigeminal angiomatosis, is the combination of a hemangioma of the skin, usually over the area of distribution of one or more branches of the fifth cranial nerve (nevus flammeus), glaucoma, and angiomatous changes in the vessels of the meninges of the brain. Nevus flammeus may be associated with glaucoma without meningeal involvement, or with a meningeal angioma without glaucoma. The incomplete forms are more frequent than the complete syndromes. When present, the facial lesion and the glaucoma almost always occur on the same side.

Numerous instances of the association of glaucoma and facial hemangioma have been reported. The syndrome has been well reviewed in the literature (Ballantyne,[1] O'Brien and Porter,[2] and Joy[3]). Nevus flammeus is usually unilateral but may be bilateral, and, when associated with glaucoma, involves the lids or conjunctiva. Glaucoma is either buphthalmic or the chronic simple type.

The ocular findings associated with nevus flammeus are dilated conjunctival vessels, vascular nevus of the conjunctiva and the episclera, peripheral anterior synechiae, heterochromia iridis, dense stroma of the iris, dilated vessels of the iris, varicose vessels of the iris, hemangioma of the iris, tortuous retinal vessels, varicosities of the retinal veins, dark red fundus, changes in the pigment epithelium of the retina, retinal detachment, dilated and tortuous choroidal vessels, hemangioma of the choroid, and cavernous atrophy of the optic nerve. The most common intra-ocular vascular change is a hemangioma of the choroid.

Choroidal hemangiomas frequently occur as isolated lesions, and are considered by Berliner[4] to be variants of the Sturge-Weber syndrome. They present a difficult diagnostic problem when observed clinically and are usually mistaken for malignant melanomas. Most globes in which angiomas of the choroid are found upon sectioning in the laboratory, are either enucleated because of suspected melanomas or because of the presence of absolute glaucoma of unknown cause.

The neurologic symptoms, which are due to intracranial hemorrhage from the abnormal vessels of a diffuse meningeal hemangioma, are listed by Anderson.[5] They are localized and generalized epileptiform seizures, hemiplegia, hemianopia, mental deficiency, contralateral homonymous hemianopia, and epilepsy.

Case Reports

The first 3 cases are clinicopathologic reports of globes examined in the L. F. Montgomery Laboratory of Ophthalmic Pathology. Cases 1 and 2 are examples of isolated choroidal hemangiomas. Case 3 demonstrates the association of nevus flammeus and heterochromia.

Case 1. D. C. B., a white man aged 30 years, was admitted to Lawson Veterans Administration Hospital, Chamblee, Georgia, July, 1947. He complained of blurred vision of the left eye of 8 weeks duration, and dull, aching headaches over the left side of his face of 4 weeks duration. He denied any previous ocular difficulties.

Past History. The patient enlisted in the Army of the United States in October, 1944. He had a ruptured peptic ulcer in January, 1945, and was discharged in March, 1945, after surgery. Following his discharge from the Army, he had daily epigastric pain with frequent nausea and vomiting, once with blood.

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*Read before the Section on Ophthalmology and Otolaryngology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

†From the Department of Ophthalmology, Emory University School of Medicine, the Grady Clay Memorial Eye Clinic, Grady Memorial Hospital, and the Eye Service, Atlanta Veterans Administration Hospital, Atlanta, Ga.

Six weeks prior to admission, he consulted a private ophthalmologist, who noted vision of the left eye to be 20/40 and the presence of a lesion near the optic disc. Upon re-examination two weeks later, there was, in addition, a serous detachment of the left retina, with a severe loss of vision. The patient was examined by three consultants, who concurred in the opinion that the lesion near the optic disc was a tumor. He was referred to the Veterans Administration Hospital for enucleation. Two weeks prior to admission, he was examined by an internist and told that he had another gastric ulcer and further surgery was necessary.

The family history was noncontributory; both parents and nine siblings were alive and well. None had any known eye disorder or unusual skin pigmentation.

Physical Examination. Examination revealed a well-developed and nourished man. The skin was clear in all areas; there were no eruptions or abnormal pigmentations. The head and neck, the ears, nose, and throat were normal. The chest, heart, and lungs were normal. Blood pressure was 120/85. There was mild epigastric tenderness. The remainder of the examination was normal.

Eye Examination. Vision in the right eye was 20/15. Vision in the left eye was 20/400. The right eye was entirely normal. The left eye showed minimal conjunctival injection. The iris was of normal color. The pupil reacted to light and accommodation. Fine vitreous opacities were seen. Adjacent to the optic disc, nasally and superiorly, there was a circumscribed solid detachment of the retina, about 2 disc-diameters in size, with an elevation of approximately 3 to 4 diopters. At the nasal side of this detachment there was a small hemorrhage. Almost the entire lower half of the retina showed a serous detachment. Visual field studies showed a loss of the peripheral portion of the superior field of vision of the left eye, and a scotoma extending inferiorly and temporally from the blind spot.

FIG. 1

(Case 1) Segmental view, showing typical location and extent of the tumor.

FIG. 2

(Case 1) Low-power view of the hemangioma of the choroid, showing cystoid changes in the retina overlying the tumor.

Laboratory Examination. There were 10,000 white blood cells, of which 71 per cent were polymorphonuclear leukocytes, 27 per cent lymphocytes, and 2 per cent eosinophils. The hemoglobin was 100 per cent. The urine was normal with a specific gravity of 1.010. The Kahn reaction of the blood was negative. X-ray examinations of the skull, chest, pelvis, and long bones, showed no defects. X-rays of the gastrointestinal tract revealed a deformity of the duodenal bulb, "consistent with an old healed ulcer."

The *clinical diagnosis* was malignant melanoma of the choroid, with detachment of the retina. The eye was enucleated on July 30, 1947. The globe was fixed in formalin 10 per cent.

Microscopic Examination. The anterior segment was normal. The anterior chamber was of average depth and the filtration angle was open. Adjacent to the optic disc and extending almost to the equator medially, there was a tumor of the choroid which consisted of numerous endothelial-lined spaces filled with blood and separated by a fine hyaline connective tissue. Chromatophores were present in the septa. Many of the blood spaces communicated with adjacent ones through interruptions in the septa. A few blood vessels were seen in the tumor. The pigment epithelium of the retina overlying the choroidal mass had proliferated and undergone metaplasia to form a thin sheet of connective tissue between the retina and the choroid. Contraction of this "membrane" appeared to have caused some folding of the retina in this area, and may have been the cause of the serous detachment. Cystoid degeneration of the outer layers of the retina overlying the tumor was evident, and the retinal vessels were dilated. The tumor was not encapsulated and faded into normal choroid peripherally. There was a pink-staining fluid in the vitreous (Figs. 1 to 4).

The *final diagnosis* was hemangioma of the choroid, with secondary retinal detachment.

Comment. The choroidal lesion, unaccompanied by similar tumors of the skin or meninges, was incorrectly diagnosed as a

malignant growth of the choroid. Case 1 shows the difficulty in the clinical differentiation of these isolated vascular lesions from melanomas of the choroid. If the lesion may be assumed to have been congenital, the angioma was completely asymptomatic for 30 years.

Case 2. C. P.* a white man aged 28 years, was admitted to the Veterans Administration Hospital, Bay Pines, Florida, in August 1949. He complained of considerable pain in the right eye.

Past History. He had the usual childhood diseases. In 1945, while on active duty in the Army of the United States, the right eye became suddenly blind. He had been hospitalized in Hawaii, California, and Alabama, because of a detached retina of the right eye; glaucoma developed later.

Physical Examination. The heart and lungs were normal. The blood pressure was 120/80. The pulse rate was 90.

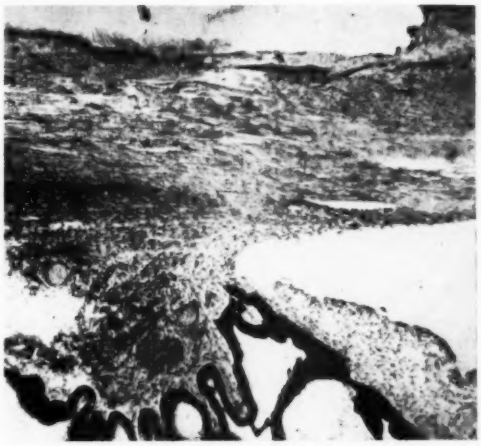
Eye Examination. The right eye was blind; vision in the left eye was 20/20. The tension in the right eye measured 40 mm. and in the left eye 19 mm. (Schiotz). There was a mature cataract in the right eye. The left eye was entirely normal.

*Dr. David Lee Mendelblatt supplied the history on this case.

FIG. 3

(Case 1) Higher-power view, showing the structure of the hemangioma and connective tissue between the retina and choroid.

FIG. 4



(Case 1) Low-power view of the filtration angle.

Laboratory Examination. There were 4,450,000 red blood cells. The hemoglobin was 90 per cent. There were 8,700 white blood cells. Bleeding time was normal. The urine was normal. A serologic test for syphilis was negative. Chest x-ray revealed apical pleural thickening, bilaterally.

The *clinical diagnoses* were: mature cataract, right eye; detached retina, right eye; absolute glaucoma, right eye.

The eye was enucleated on August 22, 1949. The globe was fixed formalin 10 per cent and sectioned horizontally. Gross examination revealed a mature cataract and a complete detachment of the retina.

Microscopic Examination. Edema of the basal cells of the corneal epithelium was evident and there were several abrasions of the epithelium. Centrally, the anterior chamber was of average depth, but the filtration angle was completely blocked by peripheral anterior synechiae. The endothelium and Descemet's membrane had grown over the false angle onto the anterior surface of the iris on each side. The iris showed atrophy with proliferation, and mild ectropion uveae was present. The ciliary body and processes were atrophic. The lens was cataractous, as shown by proliferation of the subcapsular epithelium posteriorly and liquefaction of the cortex. Extending from the optic disc laterally, almost to the equator, there was a large angioma of the choroid which consisted of spaces of varying sizes separated by connective tissue septae lined by endothelium and containing blood. Chromatophores were present in the walls. The angioma was not encapsulated and faded into normal choroid peripherally. There was a large plaque of a hyaline connective tissue which contained pigment, obviously of epithelial origin, overlying the tumor, between the choroid and retina. At one edge of this membrane there was a spicule of bone. Adhesions were seen between the retina and the choroid in the region of the angioma. Bruch's membrane appeared to be a double layer near the optic disc on the side of the tumor. The retina was completely detached by a pink-staining

fluid which contained macrophages. The entire retina was atrophic and gliosis was evident, especially in the area adjacent to the tumor of the choroid. There were excrescences of the lamina vitrea. The cribriform plate was bowed slightly outward. The optic nerve appeared to be normal (Figs. 5 to 7).

The *final diagnoses* were: hemangioma of the choroid; retinal detachment secondary to choroidal hemangioma; glaucoma secondary to retinal detachment.

Comment. This globe was similar in every respect to the previous one, with additional changes secondary to the detachment of the retina. Longstanding retinal detachments frequently result in apposition of the root of the iris to the corneoscleral trabeculum, with the formation of peripheral anterior synechiae. The tumor in the second case is a replica of that of case 1, only larger. The plaques of connective tissue usually present over these tumors may be largely responsible for these lesions having the appearance of melanomas of the choroid in cases observed clinically. This tissue would also increase the interference with transillumination when it is employed.

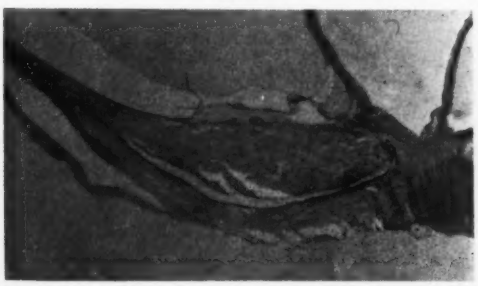
Case 3. J. M., a white man aged 63 years, was seen by an ophthalmologist for the first time a few days prior to enucleation of the eye. The attending physician has died since this operation, and the history was furnished by Dr. Stacy C. Howell, who assisted at the enucleation. The patient complained of severe pain in the left eye of several days duration.

Past History. He stated that vision in the left eye had always been defective. About 1945, he suffered some pain in the left eye, following which the vision of the eye was completely lost. The iris of the left eye had always been a darker color than the other.

Physical Examination. There was a large "port-wine" hemangioma of the skin which covered almost half of the left side of his face and ear, but did not involve the eyelids or orbital region.

Eye Examination. The right eye was normal. The left eye was soft and there was a hyphemia. Heterochromia iridis was noted; the left iris was darker than the right. There was a dense cataract.

FIG. 5



(Case 2) Segmental view, showing the hemangioma of the choroid, the connective tissue mass over the tumor, and pink-staining fluid beneath the retina.

FIG. 6

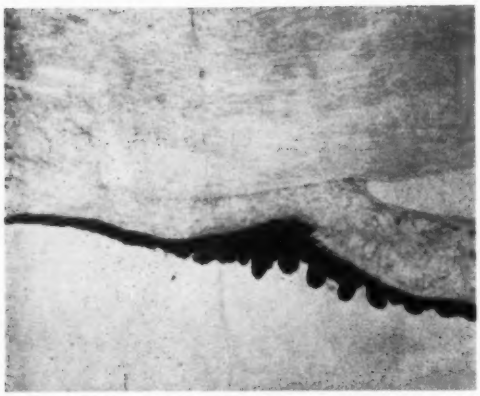
(Case 2) Higher-power view of the hemangioma, showing the connective tissue mass over the tumor.

The *clinical diagnosis* was atrophy of the globe.

The eye was enucleated on May 26, 1949. The globe was fixed in formalin 10 per cent and sectioned horizontally. Gross examination revealed a small hyphemia and a complete detachment of the retina. The subretinal fluid was firm and had a dark olive-drab color. Scattered throughout this fluid were numerous fine brownish granules.

Microscopic Examination. There was a perilimbal plasmacytic and lymphocytic infiltration. The basal cells of the corneal epithelium were edematous. There was a small defect in Bowman's membrane centrally. There were a few pigment granules in the stroma. Near the limbus, on one side, a few flecks of calcium were seen beneath the epithelium. Descemet's membrane was detached on one side by blood and a pink-staining fluid. The endothelium was atrophic. The anterior chamber was decreased in depth and the filtration angle was completely blocked by peripheral anterior synechiae. The endothelium and Descemet's membrane had grown over the fa'se angle and covered the anterior surface of the iris on each side. The filtration meshwork showed severe atrophy and contained pigment. The iris showed atrophy with proliferation. Acute and chronic inflammatory cells were seen in the iris. Occlusion and seclusion of the pupil were evident. The lens showed a hypermature cataract with wrinkling of the capsule, a large anterior polar "cataract," liquefaction of the cortex, and proliferation of the subcapsular epithelium posteriorly. There was a thick cyclitic membrane which had partially detached the ciliary body on each side. Chronic inflammatory cells, chiefly lymphocytes, were seen in the ciliary body. The retina was completely detached by a pink-staining fluid and was adherent to the cyclitic membrane. The retina was completely disorganized and gliosis was evident. Perivascular infiltration of chronic inflammatory cells of most of the retinal vessels was seen. Cholesterin slits, pigment-laden macrophages, and giant cells were present in the subretinal fluid. Atrophy of the choroid was evident. Numerous chronic inflammatory cells, chiefly lymphocytes, were present in the choroid. The choroid was detached anteriorly.

FIG. 7



(Case 2) Low-power view of filtration angle, showing closure of the angle by fibrous peripheral anterior synechiae, and a Descemet's-like membrane over the angle.

Many dilated vessels, but no angiomas, were present. A few excrescences were seen on the lamina vitrea. This membrane took a basophilic stain posteriorly. In some of the sections a small plaque of bone was present in the choroid. The cribriform plate was bowed outward and the optic nerve showed severe atrophy.

The *final diagnoses* were: uveitis; retinal detachment secondary to inflammation; phthisis bulbi.

Comment. The findings are essentially those of a severely inflamed eye. The cause of the inflammation is not readily apparent, but it is doubtful if it is secondary to a detached retina. The sequence of events appears to have been uveitis, iris bombé, blockage of the filtration angle by peripheral anterior synechiae, formation of a cyclitic membrane, and detachment of the retina. All available tissue was sectioned and examined, but no uveal vascular lesion was found.

Only one of the remaining cases to be presented showed a complete Sturge-Weber syndrome. In two other cases there were facial hemangiomas and glaucoma, but no visible choroidal lesions. The seventh case is an equivocal one, in which there was a small facial lesion and a retinal detachment.

Case 4. B. E. A., a white man aged 42 years, reported to the Eye Clinic, Lawson Veterans Administration Hospital, Chamblee, Georgia, in June 1951, because of increased haziness of the vision of his right eye. He was on active duty with the United States Army at that time.

Past History. A birthmark had always been present on the right side of his face. He had the usual diseases of childhood without sequelae. Prior to the war, he was a public school teacher. He served in the Pacific Theater of Operations from 1941 to 1945. Ten months prior to admission he had noticed a blurring of vision of his right eye for the first time, without haloes or pain. He had been examined at the Station Hospital, Fort Sill, Oklahoma, four months later, and a diagnosis of glaucoma had been made. He had not used the miotics prescribed because they increased the haziness of vision.

The family history was noncontributory; his father died at 50 years of age of "carcinoma of the abdomen," his mother was alive and well at the age of 84 years, and two sisters were alive and well. There were no familial or hereditary diseases.

Physical Examination. Examination revealed a well-developed and nourished male. The skull was symmetrical. The neck was unremarkable. There was an extensive hemangioma of the skin of the right side of his face including the eyelids and extending down to the upper lip. The ears were normal. The left nasal passage was clear, the right nasal passage was occluded by a deviated septum. Examination of the mouth was negative except for the presence of the hemangioma which extended into the mucous membrane of the right upper lip. The chest was symmetrical. The lungs were clear to percussion and auscultation. The heart was in normal position, the sounds were of good quality, the rate and rhythm were regular. Blood pressure was 120/80. The abdomen was moderately obese. No masses or tenderness were noted. The balance of the physical examination was within normal limits.

Eye Examination. The vision in the right eye was 20/20, in the left eye 20/20. The tension in the right eye measured 63 mm. and in the left eye 16 mm. (Schiotz). The right cornea was edematous. The globe was slightly congested, with dilated vessels present nasally and temporally near the limbus. The anterior chamber was of average depth and the filtration angle open (gonioscopy). The iris was normal. The pupil reacted to light and accommodation. The vitreous was clear. The optic disc was cupped; the fundus was otherwise normal. The left eye was entirely normal. Visual field studies revealed a Bjerrum scotoma in the field of vision of the right eye.

Laboratory Examination. There were 6,350 white blood cells, of which 49 per cent were polymorphonuclear leukocytes, 39 per cent lymphocytes, 8 per cent monocytes, and 4 per cent eosinophils. The hemoglobin was 14.6 Gm. The sedimentation rate was 11 mm. per hour, and the hematocrit 46. The Kahn test was negative. The urine was normal with a specific gravity of 1.028. X-ray studies of the chest and skull were negative.

Clinical Course. The intra-ocular pressure of the right eye was rapidly made normal by miotics (pilocarpine and eserin) and remained so, except on one occasion, while under observation during the following 14 months. A water-drinking test failed to elevate the pressure in the left eye, but did so to a significant figure in the right eye. Two weeks after admission a biopsy of the facial lesion was taken. The laboratory report was as follows: "The specimen consists of a fresh piece of tissue measuring approximately 1.0 cm. by 3.0 mm. The entire specimen is submitted for microscopic study. In this specimen, thin squamous

epithelium covers the section. Just beneath the surface, at one border, many vascular channels are noted. These vary considerably in size and shape. Many are filled or partially filled with red blood cells. The remaining portion of the slide is made up of skin adnexae, hair follicles, sebaceous glands and loose fibrous tissue. *Diagnosis:* hemangioma." On his last visit to the eye clinic, prior to a change of station, vision was normal in each eye and there was no increase in the size of the visual field defect.

Comment. This case demonstrates the association of glaucoma, which resembles the chronic simple type, and nevus flammeus. The filtration angle was open. The unilaterality of the condition, and its advanced state, probably indicate a secondary type of glaucoma, although an intra-ocular vascular lesion was not visible ophthalmoscopically.

Case 5. J. E. G., a white girl aged two months, was seen in consultation through the courtesy of Dr. William Edwards, of Atlanta, who also granted permission to report the case.

Past History. The child was born in May, 1955. This was the first pregnancy of the mother, aged 34 years, who was Rh positive. The pregnancy was full term. The duration of labor was slightly in excess of eight hours. Trilene anesthesia was used. The condition of the infant at birth was good; there was no asphyxia, and color and crying were normal. There was no skull or scalp injury. Examination shortly after birth revealed a "port-wine stain" of the left side of the face, including the parietal region and crossing the bridge of the nose. The eyes, ears, nose, and throat were normal. The heart, lungs, cord, anus, genitalia, and the extremities were normal. Silver nitrate 1 per cent was instilled into each conjunctival sac, after which they were irrigated with sterile normal saline. The infant was placed in an incubator for 25 minutes, 5 minutes after birth, apparently as a routine measure. Birthweight was 7 pounds. At the time of dismissal from the hospital, the mother noticed that the left pupil was dilated and the eye appeared to be slightly larger than the other.

The *family history* is significant. The father of the child has an angioma, about 3 cm. in diameter, of the skin of the right side of the neck at the angle of the mandible. His vision and fundi are normal. A paternal uncle has pigmentary glaucoma but no birthmarks; he is not available for examination. The paternal grandfather has a red "mark" on his neck.

Physical Examination. There was a pink hemangioma of the skin of the left side of the face, which extended across the midline. The general examination was as recorded above.

Eye Examination. The right eye was entirely normal. The left eye and cornea were enlarged and the cornea was edematous, as well as scarred. The tension in the right eye measured 16 mm., in the left eye 40 mm. (Schiotz). The anterior chamber was deep and the filtration angle appeared to be unobstructed (gonioscopy). The fundus was difficult to see despite the instillation of glycerin. The optic disc showed early cupping.

Laboratory Examination. Radiographic studies on July 14, 1955, were reported as follows: "There is a soft tissue swelling in the frontal area. The bony structures are normal here and elsewhere and no calcifications are seen."

Clinical Course. The intra-ocular pressure of the left eye was not reduced by miotics (pilocarpine). A corneoscleral trephine was performed by Dr. F. P. Calhoun, Jr., on September 6, 1955, who stated that the pressure became normal by the procedure.

Comment. This is an example of the association of buphthalmos and nevus flammeus, with x-ray changes suggestive of meningeal involvement. The filtration angle was open and, unless there was a defect in the drainage mechanism of the anterior chamber elsewhere, the most likely cause of the glaucoma is a uveal hemangioma.

Case 6. E. B., a white man aged 18 years, was examined in August, 1952. He planned to enter college the following month, and in order to qualify for a scholarship, an eye examination was necessary.

Past History. He first became aware of poor vision of the right eye at the age of 9 years, during a routine vision test in school. He was not seen by an ophthalmologist until the age of 15 years, however, and only then because he failed a visual test for a driver's license. He was told at that time that glasses would not help him. He had measles and mumps in childhood. In 1937, and again in 1952, he was treated for pneumonia. In 1951, he had whooping cough. A large birthmark of the right side of his face had always been present. His parents and 3 siblings were alive and well. He was not aware of the presence of similar skin lesions in the family.

Physical Examination. There was a hemangioma of the skin which covered the right side of the face, including the eyelids.

Eye Examination. Vision in the right eye was finger-counting at 6 feet, improved to 20/200 with a + 8.00 sphere. Vision in the left eye was 20/20. The tension in the right eye measured 20.1 mm., in the left eye 17.5 mm. (Schiotz). The conjunctiva and cornea were normal on each side. The anterior chambers were of normal depth and equal. The filtration angles were open (gonioscopy). The media of the right eye were clear. There was an elevation of the retina superiorly, involving almost the entire upper half, and including the macula. The inferior edge was steep and reached an elevation of 5 diopters to gradually decline until the periphery was reached. Laterally, the area extended to the periphery. The area of elevation had a dark reddish color, somewhat darker than the fundus inferiorly, with a mild pigment disturbance, namely a slight increase in pigmentation. There were two drüsen-like lesions above and lateral to the macula. The fundus was normal otherwise. The left eye was entirely normal. Visual field studies revealed a scotoma for small targets in the right field of vision which corresponded in size and position to the fundal lesion.

Laboratory Examination. Radiographic studies of the skull, on January 26, 1953, were reported as

follows: "The cranial vault has a normal configuration. In the parietal region, there are numerous, irregular vascular channels covering an area about 3.5 by 3 cm. The convolutional markings are not accentuated. There are no intracranial calcifications. The sella turcica is normal in size and shows no erosion. The paranasal sinuses and mastoid cells are clear. No abnormalities of the facial bones are seen. Impression: There is an area of increased vascularity in the parietal bone. Both meningioma and hemangioma should be considered."

Clinical Course. Because this patient presented the unique opportunity to observe clinically an eye with an obvious choroidal angioma, certain studies were made in an effort to determine, if possible, the mechanism of the glaucoma which, while absent now, would be expected to appear eventually. The following observations were made during the 22 months following the initial visit. The intra-ocular pressure in the right eye usually measured 2 to 5 mm. lower than that of the left but both were always within normal limits. The pressure was not influenced by mydriatics of any kind. The rate of aqueous outflow, as determined on several occasions, was normal in each eye. A water-drinking test did not cause a significant elevation of pressure in either eye. Therefore, it appeared that the "outflow" mechanism of the anterior chamber of each eye was normal. The jugular compression test was performed on several different occasions. Whenever a sphygmomonometer cuff was placed about the neck and inflated to 60 mm. of Hg., the pressure in the right eye invariably rose to a level of approximately 30 mm. Hg., or more. To demonstrate, in table 1 there are three recordings of the rise in the intra-ocular pressure during such tests.

During these tests, the facial angioma became livid, and with the production of glaucoma, the right eye became painful. These effects disappeared when the jugular compression was released. Observation with the ophthalmoscope during such tests failed to reveal a perceptible increase in the size of the fundal lesion; nor was there any obvious forward shift of the iris —lens diaphragm.

Comment. The facility with which glaucoma is produced in an eye which contains a hemangioma of the choroid when jugular compression is applied, indicates that the mechanism must be one capable of functioning instantly. During the period of compression, uveal drainage through the vortex veins is blocked as is the drainage of aqueous into the anterior ciliary veins. Blocking the outflow of blood from the choroid and the angioma increases the bulk of the choroid sufficiently to increase the intra-ocular pressure suddenly. The jugular compression test would appear to be an important diagnostic aid, especially in young adults, in differentiating vascular lesions in the choroid from other tumors. The choroidal lesion in this case had no characteristics which would be helpful in recognizing it clinically. As a matter of fact, the area of suspected angioma, except for increased darkness and elevation, resembled the remainder of the fundus. The two drüsen-like lesions were most certainly areas in which the pigment epithelium had proliferated to form plaques similar to those seen histologically in cases 1 and 2.

Case 7. R. J., a white girl aged 17 years, was examined in May, 1954, because of a large exotropia. She had grown increasingly conscious of the cosmetic blemish caused by the squint and requested surgical correction.

Past History. The vision of the left eye had always been extremely bad, and for the past several years the left eye had diverged. There was no history of trauma to the eye or of eye disease. Her mother had a large "birthmark" of the entire left side of her face and neck, which extended down to the level of the left breast.

Physical Examination. There was a brownish non-elevated discoloration about 1.5 cm. in diameter on the left side of the chin. Otherwise, the head and neck were normal. The blood pressure was 120/70. The heart and lungs were normal. The abdomen and extremities were normal.

Laboratory Examination. There were 10,700 white blood cells, of which 73 per cent were polymorphonuclear leukocytes, and 27 per cent were lymphocytes. The hemoglobin was 12.5 Gm., or 80.6 per cent. The coagulation time was normal. The urine was normal with a specific gravity of 1.001.

Eye Examination. The vision in the right eye was 20/20, in the left eye, light perception. The tension in the right eye measured 25.6 mm., in the left eye 22.3 mm. (Schiotz). There was an exotropia of approximately 35 diopters. The right eye was normal. In the left eye there were vitreous opacities, the in-

TABLE 1

	Initial Pressure	*30 sec.**	*60 sec.**	*90 sec.**	*120 sec.**	*2 min. after release of pressure on neck*
September 1952						
Tension right eye	11.9 mm.	23.4 mm.	32.0 mm.			
Tension left eye	10.0 mm.	22.3 mm.	22.3 mm.			
October 1952						
Tension right eye	14.0 mm.	29.0 mm.	33.1 mm.			14.0 mm.
Tension left eye	19.4 mm.	19.4 mm.	19.4 mm.			19.4 mm.
June 1953						
Tension right eye	5.7 mm.	23.0 mm.	26.5 mm.	23.0 mm.	23.0 mm.	
Tension left eye	14.4 mm.	(Not recorded. No significant elevation.)				

*Time in seconds indicate elapsed time since cuff was inflated to 60 mm. Hg.

ferior half of the retina was detached, up to and including the macula, and cystoid degeneration of the macula was evident. No retinal tears were visible.

The *diagnoses* were: retinal detachment, serous; exotropia.

Clinical Course. Because of the unexplained retinal detachment, the presence of the small angioma on the chin and a very extensive one on the face, neck, and chest of her mother, the jugular compression test was performed. The results were almost as striking as those obtained in the previous case,—the pressure in the right eye remaining normal, that of the left eye rising from 22.3 mm. to 33.1 mm. (Schiotz) in 60 seconds. Because of reluctance on the part of the patient, the test was not repeated. Operation on the extra-ocular muscle was done in July 1954.

Comment. Compression of the jugular veins for one minute caused the intra-ocular pressure in one eye to rise to a glaucomatous level, possibly indicating the presence of a uveal vascular lesion in the eye. The pressure in the other eye was unaffected.

Summary and Conclusions

Six cases of partial or complete Sturge-Weber syndrome are presented. Nevus flammeus was present in four of the cases. In one, nevus flammeus was associated with buphthalmos, in another, with glaucoma resembling chronic simple glaucoma, in another, with an ophthalmoscopically visible hemangioma of the choroid and a radiographically demonstrable meningeal lesion, and in another, with heterochromia. Glaucoma was found in four of the cases, but in none could the glaucoma be directly attributed to a vascular anomaly of the uvea. In two of these cases, the glaucoma appeared to be due to secondary changes following long-standing retinal detachment with blockage of the filtration angle. In the two patients observed clinically with glaucoma, the filtration angle was open in each, but a vascular lesion was not seen in either. However, if the fundal lesion in case 6 is a hemangioma of the choroid, it would not be difficult to overlook a similar but smaller lesion on ophthalmoscopic examination. In none of the cases were there neurologic symptoms.

The acute rise in the intra-ocular pressure in an eye which is suspected of containing a hemangioma of the choroid when the jugular veins are compressed, indicates that disorganization of the fluid traffic of the uvea plays an important role in the production of the glaucoma. Blockage of the vortex veins, with a sudden increase in the bulk of the choroid and of the hemangioma, appears to be the essential factor in causing the elevation of pressure. The test is suggested as a possible diagnostic aid in differentiating hemangiomas of the choroid from malignant melanomas, especially in young adults.

References

1. Ballantyne, A. J.: Buphthalmos with Facial Nevus and Allied Conditions, Brit. J. Ophth. 14:481, 1930.
2. O'Brien, C. S., and Porter, W. C.: Glaucoma and Nevus Flammeus, Arch. Ophth. 9:715, 1933.
3. Joy, H. H.: Nevus Flammeus Associated with Glaucoma, Am. J. Ophth. 33:1401, 1950.
4. Berliner, M. L., and Breinin, G. M.: Angioma of the Choroid, Arch. Ophth. 46:39, 1951.
5. Anderson, J. R.: Hydrophthalmia or Congenital Glaucoma, London, Cambridge University Press, 1939.

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Experiences in the Management of Thyroid Disease: Six Hundred and Eighty-four Cases Treated in a Ten Year Period*

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The authors have analyzed their clinical material in terms of the incidence of malignancy, and the best methods of therapy.

AN EVOLUTIONARY ERA IN THE MANAGEMENT OF THYROID DISEASE was ushered in some 10 years ago by the introduction of certain chemical agents and, a little later, radioactive iodine which control thyrotoxicity. However, with the unfolding of time and events over this exciting decade, this change in modality has served wisely to modify the indications for, but obviously not to replace, the surgical management of goiter.

The literature abounds with reports of the character and behavior of enlargements of the thyroid gland. It seems extremely difficult for various observers to meet upon a common ground with respect to their management. This honest difference in opinion prompted a recapitulation and evaluation of the management of a sizable group of cases under my direction.

The series of 684 cases from which evidence is presented here, comprises two groups. In Group I, there are 346 unselected private patients. In Group II, there are 338 selected or referred service patients who were treated at the University of Oklahoma Hospitals. These cases accrued over the last decade, from 1946 to 1955.

Prior to the initial use of I^{131} at the University of Oklahoma Hospitals in 1952, both groups, irrespective of classification were treated by surgery. During the period of 1952 to 1955, 18 patients in the series were treated solely with I^{131}.

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Clinical Data

A compilation of data from our study discloses several points.

Age Distribution. As will be seen in figure 1, there has been an increase in the incidence of goiter, in a nonendemic goiter area of the Southwest, in the fourth, fifth, and sixth decades of life.

Clinical Classification. Of the 684 cases of goiter 340, or approximately 50 per cent, were toxic and 209, or 61 per cent of these, were diffuse in nature. Many of the glands showing clinically solitary nodules were later found to be multinodular and no distinction was made between the two, in the final classification. We found a high incidence of thyroiditis in the final classification.

The ratio of female to male patients was 6 to 1 (Table 1).

Incidence of Malignancy. In table 2 are listed the types of malignancy and the incidence encountered in our series of cases. They were:

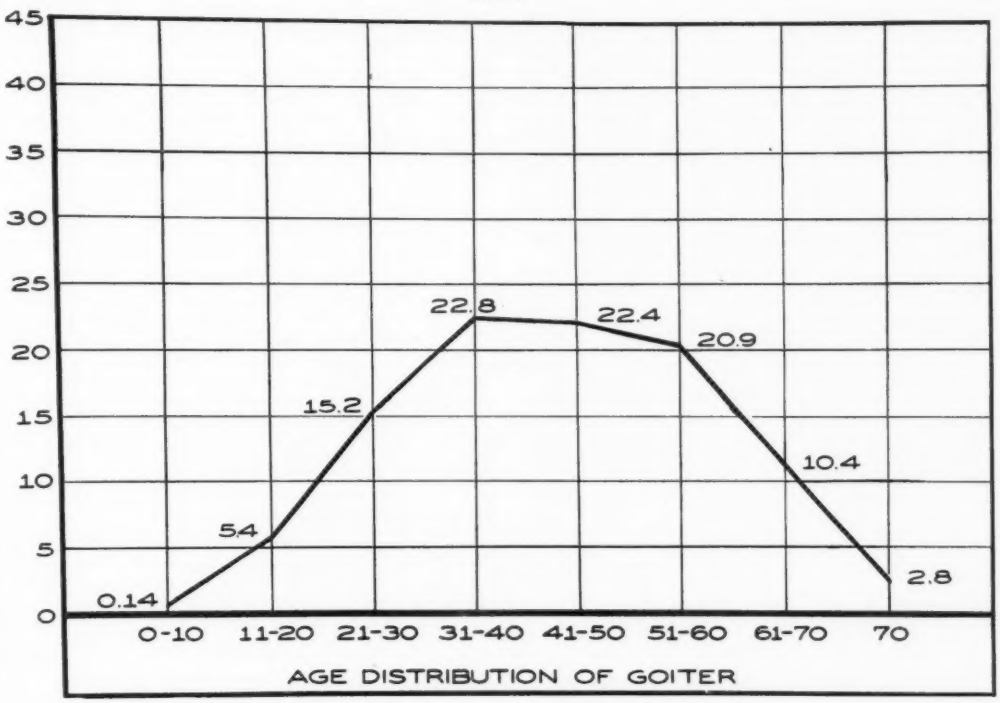
Papillary	Reticulum cell
Alveolar	Liposarcoma
Small cell	Epidermoid carcinoma
Benign metastasizing	Follicular
Hürthle cell	Solid

Undetermined

In this series of 684 cases, 33 or 4.8 per cent had a malignant process in the thyroid gland. Adenocarcinoma (12 papillary, 7 alveolar, 1 follicular) accounted for 60 per cent of the malignancies. Sarcoma accounted for 9 per cent, which is somewhat contradictory to that of 1 per cent reported by other investigators.

In those having a malignant process, there

FIG. 1



The age distribution of goiter, irrespective of classification.

were 23 females and 10 males, a sex ratio of 2.3 to 1.

The incidence of malignancy in each age group is listed in table 2. The youngest patient, an 11 year old white girl had papillary adenocarcinoma. The oldest, an 84 year old man, had a Hürthle cell carcinoma. Adenocarcinoma is not unusual in any age group. In our series, the peak incidence occurred in the 30 to 40 age group. The peak *per patient* incidence (37 patients having 3 instances of malignancy) occurred in patients under 20 years of age (Fig. 2).

Therapeutic Management

The treatment of thyroid disease seems to center about its management by surgical means, antithyroid drugs, and by the newest agent, radioactive iodine.

The danger in conservative therapy is well emphasized in recent reports in the literature which stress the incidence of malignancy in various types of glands. In the solitary nodular goiters, the reported incidence of malignancy varies from 2.5 to 25 per cent, according to various authors. In the clinically multinodular goiter, this incidence varies from 4 to 10 per cent.

In our series, the incidence of malignancy in the nodular toxic and nodular nontoxic goiters (solitary nodule included) was 11 per cent. This is too great to justify the risk of nonoperative management. In all goiters, the incidence of malignancy was 4.82 per cent.

That thyroidectomy is no assurance against the subsequent development of carcinoma of the thyroid gland is well borne out by the fact that 9, or 27 per cent, of the cases of malignancy in our series had, at some previous time, undergone thyroidectomy.

TABLE 1

CLINICAL CLASSIFICATION OF 684 CASES OF GOITER

Clinical Diagnosis *598 Females, 86 Males, A Ratio of 6-1*		
Type	*Number of Cases*	*% of Total*
Nontoxic diffuse	36	5.25
Nontoxic nodular	262	38.3
Toxic diffuse	209	30.55
Toxic nodular	131	19.15
Chronic thyroiditis	46	6.72

TABLE 2

INCIDENCE OF MALIGNANCY IN GOITERS OF RESPECTIVE AGES

		Malignancy												
Age (Yrs.)	*Cases*	*PC*	*AC*	*SCC*	*BM*	*H*	*RTCS*	*LIPS*	*EPPCA*	*FOLC*	*SOL*	*UND*	*Total*	*% of Malig. Cases*
0-10	1													0
11-20	37		1			1				1			3	8.1
21-30	104			1									1	0.96
31-40	156	5	3										8	5.1
41-50	153	3	2										5	3.2
51-60	143	3	1	1	1		1	1			1	1	10	7
61-70	71	1			1			1	1				4	5.6
70	19					2							2	2.7
Total	684	12	7	2	2	3	1	2	1	1	1	1	33	4.8

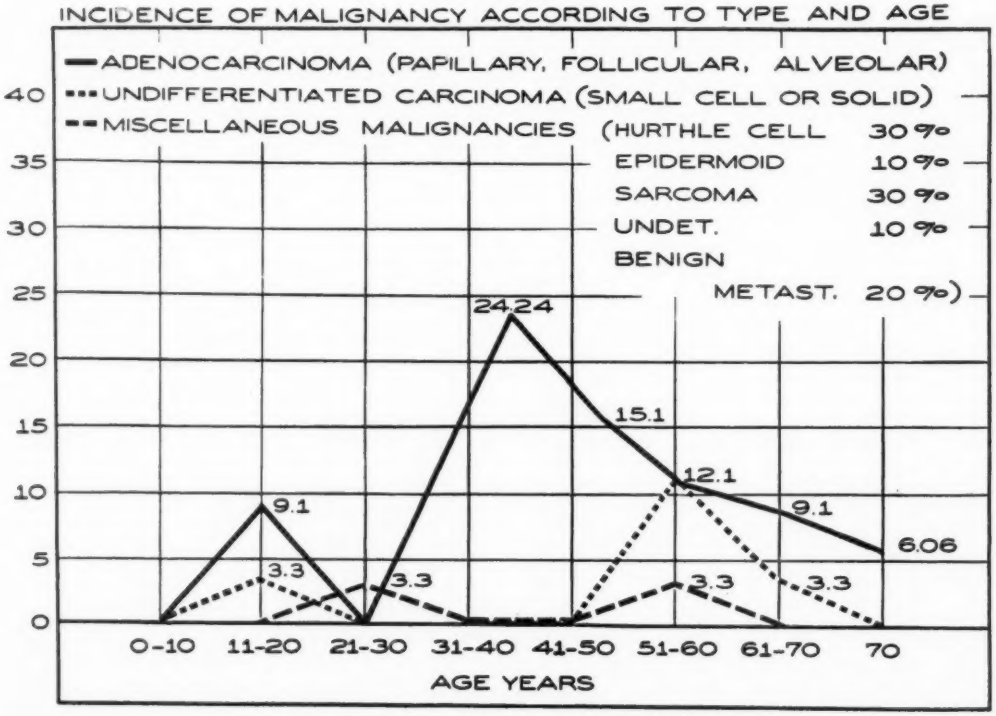
Although carcinoma is rarely reported to arise in toxic goiter, such instances have been reported and it is noteworthy that 2 of the 33 cases of malignancy in our series arose in such glands. Also, 5 instances of malignancy were found in diffuse nontoxic goiters.

The development of carcinoma in a focus of thyroid tissue, in a clinically diffusely enlarged gland is illustrated by the following case in our series.

Mrs. T. C. B., a 40 year old woman, gave a history of bilateral enlargement of the thyroid. Examination revealed bilateral diffuse enlargement of the gland but there was no evidence of toxicity. There was no lymphadenopathy and the remainder of the examination was unremarkable. Hemogram and urinalysis were within normal limits.

At operation, a grossly diffuse enlargement of both lobes of the thyroid was confirmed. Each lobe was about 8 by 6 cm. in size. There was no adherence to surrounding structures and no lymphadenopathy was present. A subtotal removal of both lobes and excision of the isthmus was done.

FIG. 2



Percentage comparison of types of malignancy in the various age groups.

Pathologic examination of the specimen revealed the presence of a focus of papillary projections adjacent to hyperplastic thyroid tissue. The diagnosis was papillary adenocarminoma (Fig. 3).

An important factor in determining the probable incidence of malignancy in any group or series of cases is the examiner's inability to accurately detect single or multiple nodules. Included in our series of patients, operated on between 1952 and 1955, were 17 cases classified as solitary adenomas and 32 classified as unilateral nodular glands. To our amazement, careful correlation disclosed nonconformity in the clinical and gross and/or microscopic classification in 40.8 per cent of the cases. This illustrates the hazard of relying on clinical nodularity as a criterion for the choice of therapy.

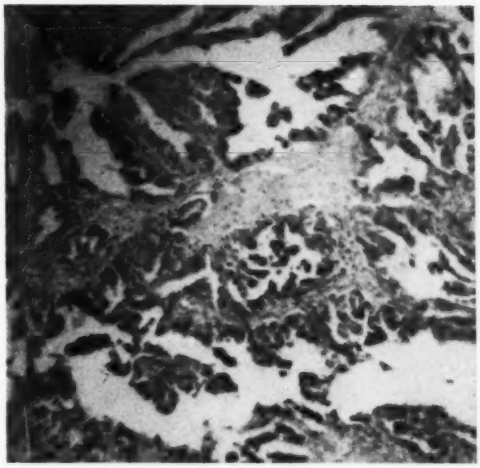
Although the indications for operations on the thyroid have wisely been modified in the past decade, and perhaps curtailed to a certain degree, the operation of thyroidectomy has, over the years, demonstrated its worth and importance. It is a well conceived step by step development which will remain paramount in thyroid management. Improvement in anesthesia and in preoperative preparation have made it an exact procedure with low morbidity and low mortality.

The nonoperative management of goiter was first acclaimed by the introduction of thiouracil derivatives. Experience has since taught us that there are certain instances in which attempts at treatment by thiouracil are indicated, and more and more we are becoming convinced that propylthiouracil and Tapazol serve very valuably in the surgeon's armamentarium. Especially, are they helpful in creating remissions in the toxic gland preliminary to surgery. However, caution in the administration of these drugs must be emphasized.

In addition to the commonly recognized potential systemic dangers from toxic effects of the drug, I should like to cite two cases illustrating other ill effects. The first is that reported by Aaron, Scheierson and Siegel,[1] the occurrence of a goiter in a newborn infant, due to the mother's ingestion of propylthiouracil.

The second is that of a 29 year old white woman in our series, who had diffuse thyroid enlargement and toxicity since May, 1954, was controlled by propylthiouracil, 300 mg. per day until October 10, 1955. She became pregnant in September, 1954, and in

FIG. 3



Thyroid carcinoma in a clinically diffuse gland.

April, 1955, while on therapy, had a spontaneous miscarriage of a stillborn child with a tremendous, diffusely enlarged thyroid gland. (The patient had a thyroidectomy one week ago.)

Although radioactive iodine constitutes an acceptable nonoperative method of treatment for diffuse toxic goiter, the indications for its use are, in general:

1. The presence of a diffusely enlarged toxic gland, as shown by an increase in the basal metabolic rate, increase in the radioiodine uptake of the gland, and/or an increase in the protein-bound iodine level of the blood.
2. Elderly patients of poor surgical risk.
3. The presence of associated diseases making surgical extirpation hazardous.
4. Recurrent or persistent hyperthyroidism which enhances surgical technical difficulties,—as injury to nerves, parathyroid deficiency, etc.
5. Sensitivity to antithyroid drugs preventing preliminary preparation for operation.
6. Failure to respond to antithyroid drugs.
7. Patient's refusal of surgery.

Since 1952, 18 patients, having nonmalignant toxic goiters, in our series were treated with I^{131}. The youngest was 29, the oldest was 73 years of age. The mean age of all patients treated was 53.3 years. The dose varied from a single one of 3 millicuries to a cumulative dose of 50 millicuries over a two year period.

A satisfactory result, shown by a reversion of laboratory signs of toxicity to normal values, a sense of well-being in the patient, and regression of the goiter was noted in 16 of the 18 patients so treated. The series of cases is admittedly small and it is much too soon to venture an evaluation of the undesirable effects and results from this method of therapy. However, to date one patient is improved but retains toxic findings and symptoms, and one patient died of superimposed disease. Malignancy has not developed in any of the group to date.

By comparison, 209 cases of diffuse toxic goiter were treated surgically. Complications occurred in approximately 5 per cent of the service patients. No complications occurred in the private patients. The over-all mortality from operation or its complications was less than 1 per cent. In the light of our studies, surgery offers greater assurance of permanent control, a shorter period of restoration, and a minimum of untoward results.

Radioactive iodine is a valuable therapeutic aid in the palliative management of certain cases of thyroid carcinoma beyond surgical removal, with or without, distant metastasis. Especially is this true in those patients with a high I^{131} uptake. Its limitations, however, are stressed by Russo and Mathews,[2] who reported 13 patients having malignant disease of the thyroid, treated with radioactive iodine. In only two patients were there gratifying results. Four of the patients had subjective improvement although the clinical course of the disease was unaltered.

The recent development of a competent team of internists, radiologists, surgeons, an endocrinologist, and a physicist at the University of Oklahoma Hospitals has served to stabilize the criteria for the management by radioiodine of selected patients with thyroid disease.

Summary

1. A study of 684 cases of thyroid disease has been presented and analyzed.

2. Three types of thyroid management have been discussed.

3. Twenty years ago, surgery dictated the removal of nodular goiters because of the incidence of malignancy arising in such glands.

4. While malignancy shows a greater affinity for nodular glands, it does not always follow a conformative pattern.

5. Obscure nodules in a diffusely enlarged gland may be clinically undetectable.

6. Adequate subtotal thyroidectomy is mandatory in all nodular goiters.

7. Radioactive iodine is an accepted method of treatment for diffuse toxic goiter. However, if no contraindications exist, definitive surgery offers distinct advantages.

8. If nodularity is observed following therapy with radioactive iodine, immediate operation is in order.

9. Enlargements of the thyroid gland inescapably place them in the category of tumors, and the principles of good cancer surgery bind themselves to thyroid tumors as well as to other types of tumor.

References

1. Aaron, H. H., Scheierson, S. J., and Siegel, E.: Goiter in Newborn Infant Due to Mother's Ingestion of Propylthiouracil, J.A.M.A. 159:848, 1955.
2. Russo, P. E., and Mathews, H. H.: Cancer of the Thyroid Gland: Our Experience with Radioactive Iodine, South. M. J. 48:937, 1955.

Spontaneous Rupture of the Esophagus*

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The syndrome of esophageal rupture is to be differentiated from a number of diseases, among which myocardial infarction is prominent. The diagnosis must be made on clinical considerations. Only the surgeon can save the patient's life.

PERFORATION OF THE ESOPHAGUS following intrinsic esophageal disease or extrinsic trauma, e.g., erosion, impaction of a foreign body, or instrumentation, is a well-recognized entity. Rupture of a previously normal esophagus, however, is often not recognized and, in fact, the diagnosis is frequently not considered. This is particularly unfortunate since modern surgical technics make it possible to save many patients with this condition which is invariably fatal without early diagnosis and prompt surgical intervention.

About 160 cases of spontaneous rupture of the esophagus have been described in the world literature to date, but it is our opinion that the true incidence is greater, and that the diagnosis will be made more frequently as knowledge of this fatal calamity is increased. Some fatal cases diagnosed clinically as acute pancreatitis, ruptured aneurysm, or myocardial infarction, without autopsy confirmation, may well have been cases of spontaneous rupture of the esophagus.

In order to stress the importance of the clinical characteristics of this acute emergency, and to emphasize the importance of early diagnosis and treatment, three cases are reported.

Case Reports

Case 1. (Hospital No. 15-427.) A 54 year old, white farmer was admitted to the hospital complaining of severe epigastric and back pain with associated vomiting of approximately 6 hours duration. After eating breakfast he became nauseated and vomited the food just eaten and about a half cupful of bright red blood. He then immediately developed severe epigastric pain which radiated through to the middle of his back. The pain and vomiting persisted to the time of admission. *Past history* was negative except for episodes of epigastric pain coming on during meals 2 to 3 times a year over a 20 year period, each attack lasting about 24 to 36 hours and relieved by large doses of atropine.

Physical examination on admission revealed an obviously ill, middle-aged, white man in shock. He was described as thrashing about in bed and hyperventilating during the examination. Temperature was 101.4°, pulse 110 per minute and blood pressure 82/48. The heart and lungs were essentially negative. The abdomen was flat with definite spasm throughout, especially in the epigastrium and along the right costal margin. There was no rebound tenderness and peristaltic sounds were normal.

Special Studies. On admission, the Hgb. was 13 Gm., WBC 15,500, with 88 per cent neutrophils and 12 per cent lymphocytes. Chest x-ray film revealed both domes of the diaphragm to be high, slight increase in lung markings, a normal sized heart and no evidence of aneurysm. An x-ray film of the abdomen showed no evidence of obstruction and there was no free air in the abdomen. The electrocardiogram showed nonspecific T-wave changes.

A *diagnosis* of perforated peptic ulcer was made and an exploratory laparotomy was done on the evening of admission. At operation no perforation or disease was found in the abdominal gastrointestinal tract. The patient withstood the operative procedure satisfactorily although his condition remained poor. The following day fluid was noted in the right pleural cavity and it was then that the possibility of perforation of the lower esophagus or perforation of a herniation of the stomach was considered. Repeated thoracenteses were required and on the second postoperative day a catheter was left in the pleural cavity. Each thoracentesis produced from 300 to 600 cc. of fluid, which at first was serosanguinous, but subsequently the fluid resembled gastric content and a small amount of bile was noted in the pleural fluid. No operative procedure was thought justified and the patient was given symptomatic and supportive treatment until his death on the fifth day of hospitalization.

Postmortem examination revealed a small laceration on the left anterolateral aspect of the lower esophagus about 3 to 4 cm. above the cardia.

Case 2. (Hospital No. 64-021.) A 61 year old, colored man was admitted to the hospital complaining of severe, steady midepigastric pain and frequent vomiting of 4 hours duration. One year previously he had been treated at this hospital for Laennec's cirrhosis and essential hypertension, but had remained in good health until four days before admission. At that time he began to have loose, diarrheal stools following a dose of "Ex-Lax," and this continued to the time of admission. On the morning of admission he was seen

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FIG. 1

The line passes through the esophageal rupture.

by his physician because of the diarrhea, and while in the physician's office he became nauseated and vomited what was reported to be normal gastric contents. Following the vomiting the patient suddenly developed a severe, steady midepigastric pain which quickly increased in severity and soon radiated to the back. The nausea and vomiting continued, along with the pain, up to the time of admission.

Physical examination on admission revealed a well-developed, moderately obese colored man who appeared acutely ill and complained of severe abdominal pain. He was alert, rational and cooperative. The temperature was 98.4°, pulse 108 per minute, respirations 44 per minute and blood pressure 180/95. Auscultation of the lungs revealed a few scattered rales at the left base, but they were otherwise negative. The heart was moderately enlarged to the left and a Grade II, blowing, systolic murmur was heard at the apex and base. The abdomen was markedly distended, there was moderate epigastric tenderness to deep palpation and generalized muscle spasm was noted. No rebound tenderness or abnormal bowel sounds were noted. The liver edge was felt 4 finger-breadths below the right costal margin and was slightly tender. The spleen was not palpable and there was no evidence of abdominal fluid. Rectal examination was negative except for dark blood on the examining glove.

Special studies on admission showed a Hgb. of 9.7 Gm., hematocrit of 30, WBC 6,500 with 72 per cent neutrophils and 28 per cent lymphocytes, blood urea nitrogen of 17 mg., and blood sugar 300 mg. per 100 cc., a normal CO_2 and serum electrolytes, and a serum amylase of 88 Bodansky units. Chest x-ray film on admission was reported as suggestive of a pneumonitis in the left lower lung field with a slight amount of fluid in the left pleural space.

Course. The initial impression was acute pancreatitis and the usual symptomatic and supportive treatment was started. There was slight improvement initially, but during the second and third days he was noted to have some respiratory difficulty and finally developed definite signs of left pleural effusion. On the third hospital day 790 cc. of a cloudy yellow fluid were removed from the left pleural space, having a specific gravity of 1.020, an amylase of 80 Bodansky units, a total protein of 3.7 Gm. per 100 cc. and a cell count of 400 white cells per cu. mm. There was no growth on culture of this fluid. The following day 1,200 cc. of a similar fluid were removed from the left pleural space with resulting respiratory improvement. The patient was continued on intensive supportive treatment with massive doses of antibiotics, Wangensteen suction, parenteral fluids and blood transfusions, but his condition gradually deteriorated. On the seventeenth day of hospitalization gastric contents were noted in the pleural fluid and rupture of the distal esophagus was demonstrated by x-ray examination, using a thin solution of radiopaque oil (Iodochlorol). Closed suction of the left pleural cavity was then started and later an exploratory laparotomy and gastrostomy were performed. The patient appeared to withstand the procedure well for the first few hours after operation, but during the latter part of the evening he developed pulmonary congestion and expired suddenly.

Autopsy revealed necrotic exudate surrounding the lower esophagus. At approximately 4 cm. above the cardia on the left anterior wall, a small, 0.5 cm., longitudinal opening through the mucosa was seen (Fig. 1). The borders were smooth, sharp and without evidence of inflammatory thickening. A fine longitudinal gray scar extending a short distance toward the cardia was associated with this opening. There was no other evidence of disease of the remainder of the gastroin-

FIG. 2

The probe is passed through the fistula from the esophageal perforation to the left pleural cavity.

testinal tract. Microscopic examination of the esophagus revealed a sinus tract extending entirely through the lower esophagus. Other sections of the esophagus taken from areas adjacent to the rupture showed no significant pathologic change. There was no evidence of pancreatitis.

Case 3. (Hospital No. 71-016.) A 64 year old, colored man was admitted to the hospital complaining of excruciating abdominal pain and frequent vomiting of 12 hours duration. There is no record of which came first,—the vomiting or the pain. The patient was in a shock-like state on admission and it was difficult to obtain the history from him since talking increased the pain. Apparently he had vague burning upper epigastric pain with an occasional episode of vomiting and an occasional dark stool during the week prior to admission.

Physical examination on admission revealed a thin, elderly colored man who was sweating profusely, was cold and clammy, and was thrashing about in bed, grunting with each respiration. The temperature was 96°, pulse 126 per minute, respirations 22 per minute and blood pressure 82/76. There was absence of breath and whispered voice sounds over the left chest posteriorly from the sixth rib to the base. Heart sounds were weak, distant and rapid, but no arrhythmia, murmur or friction rub was heard. The abdomen was board-like with tenderness to deep pressure in the entire epigastrium. No peristaltic sounds were heard. Rectal examination was negative.

Special studies revealed a Hgb. of 14.7 Gm., WBC 7,800, with 79 per cent neutrophils and 21 per cent lymphocytes. Serum amylase was 30 Bodansky units. The electrocardiogram revealed a sinus tachycardia. A film of the abdomen in upright position showed the stomach to be distended with food and fluid; no free air was seen. Chest x-ray film revealed a hydropneumothorax on the left side.

Course. The patient was given supportive treatment, but there was no improvement in his condition and he was considered unable to stand operation. He expired 4 hours and 45 minutes after admission.

At *autopsy* a moderate amount of subcutaneous emphysema on the left side of the neck was noted. The mediastinal tissues were quite edematous, gray and friable, but there was no mediastinal shift. The left pleural cavity contained approximately 1,200 cc. of turbid, thin, brownish-gray fluid and the left pleura was dull and dirty in appearance. A 3 cm. longitudinal perforation was seen on the left anterior aspect of the esophagus approximately 3 cm. above the cardia. There was a poorly developed necrotic fistula between the esophageal perforation and the left pleural cavity (Fig. 2). The remainder of the esophagus was normal. Except for a large area of subserosal hemorrhage at the cardia of the stomach, the remainder of the gastrointestinal tract was not remarkable.

Discussion

Rupture of the esophagus is caused by a sudden increase in intra-esophageal pressure, usually associated with vomiting. The tear may be transverse and complete, but is usually longitudinal, about 1 to 8 cm. in length. The usual site is just above the cardia on the left lateral wall since the esophagus is less well supported here, and is more easily dilated.

The salient features of spontaneous rupture of the esophagus are so constant and characteristic, albeit with minor variations, that it has been diagnosed from a telephone conversation by one familiar with it. The majority of cases occur in middle aged or older men who have eaten or drunk excessively and then have retching or vomiting, occasionally self-induced. There is then sudden, severe, violent epigastric or precordial pain, often with the sensation that something has given way or torn. The pain is made worse by swallowing, and becomes increasingly severe and wider in radiation as increasing amounts of gastric contents are spilled into the chest.

The patient is invariably acutely ill, is often unable to talk because of pain, and may frequently groan involuntarily. He may lie motionless with knees drawn up, or may writhe with pain. He is pale and anxious, and either has, or develops dyspnea, orthopnea and cyanosis. Various degrees of shock are usually present. He may be hoarse as a result of increased mediastinal pressure. An invariable and early sign is the appearance of mediastinal emphysema which, in a large majority of cases, dissects into the subcutaneous tissues of the neck and upper chest. There is a rapidly developing hydropneumothorax, usually on the left side, but is often bilateral. There is rigidity and tenderness of the upper abdomen. Examination of the pleural fluid may demonstrate hydrochloric acid and food particles.

An x-ray film of the chest will show air in the mediastinum and/or a hydropneumothorax. An esophagopleural fistula can be demonstrated by lipiodol, or a dye can be given by mouth and recovered in the pleural fluid.

The usual differential diagnoses to be considered are. above the diaphragm: acute myocardial infarction, dissecting aneurysm, pulmonary infarction, and spontaneous pneumothorax; below the diaphragm: rupture of a peptic ulcer, acute pancreatitis, acute gallbladder disease, renal colic, dissecting aneurysm and ruptured spleen. A consideration of the characteristic features of this condition,—history of vomiting followed by pain, the rapid development of dyspnea, cyanosis and shock,

and the later development of subcutaneous emphysema and hydropneumothorax, should quickly lead to the correct diagnosis. The findings of food particles or hydrochloric acid in the pleural fluid, or the demonstration of an esophagopleural fistula are, of course, pathognomonic.

The importance of early diagnosis and the institution of appropriate surgical treatment cannot be overemphasized. The mortality in spontaneous rupture of the esophagus approaches 100 per cent in untreated cases within the first 24 to 48 hours. Vital time is lost, and the condition of the patient invariably deteriorates if a period of watching and waiting is decided upon, or if studies are planned over a period of days. Furthermore, early operation is in itself one of the most effective resuscitative measures in this condition, and should not be unduly delayed once the diagnosis has been established.

Summary

Attention is called to the importance of early diagnosis in the effective treatment of spontaneous rupture of the esophagus, and the classical characteristics of this condition are discussed.

Three cases of spontaneous rupture of the esophagus are reported.

Surgical Treatment of Ulcerative Colitis: Problems of the Ileostomy*

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In many patients having ulcerative colitis there comes a time when surgical interference must be considered. The indications and methods of attack are presented by the authors. It appears much is to be said for a one-stage ileostomy and colectomy for acute exacerbation of ulcerative colitis.

IT IS NOT SURPRISING that the treatment of ulcerative colitis remains controversial. This is a disease the etiology of which, despite numerous theories, remains unknown. Its course noted for chronicity is marked with exacerbations and remissions. It is a disease influenced by bacteriologic, endocrinologic, psychologic, neurologic and probably other factors. There have been, and doubtless will continue to be, numerous conflicting opinions regarding its medical and surgical treatment.

The medical treatment of ulcerative colitis has seen many variations. Attention to nutrition through proper diet, and the relaxation of the patient and the smooth muscle of his intestinal tract remain important. The use of antibiotics has proved helpful in controlling secondary infection but has failed to cure the disease. The use of corticosteroids has been advantageous in acute exacerbations and in preparation of the patient for surgery. They also fail to effect permanent cure of ulcerative colitis and definite hazards accompany their use. Psychotherapy,[1] treatment with isoniazid[2] and other modes of therapy have their advocates. Medical treatment of ulcerative colitis, nonetheless, in most cases remains palliative rather than curative. Proper surgical treatment is curative in a large percentage of patients. The mortality rate following definitive surgical treatment for chronic ulcerative colitis can be reduced to below 3 per cent and is no longer prohibitive. The morbidity, however, particularly that associated with ileostomy still exerts considerable influence on the opinions of many concerning the proper role which surgery should play in the treatment of this disease. This is the first controversial point to be considered.

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Indications for Surgical Treatment

The surgical treatment of ulcerative colitis has, of necessity, been inseparably linked with problems of the ileac stoma. The attitude of many toward the ileostomy is reflected by that of Bargen[3] who feels that success of surgical treatment is still sharply limited by these problems, and that until these can be better solved surgical treatment should be advised only when complications have developed. These complications include pseudopolyposis with its 12 per cent or greater risk of malignant degeneration, obstruction, perforation, fistula formation, perianal sepsis, carcinoma, progressive arthritis, hepatic damage and rarely massive hemorrhage.

The difficulties encountered in the past may justify such conservatism. On the other hand, many feel that improvements in the technic of ileostomy and care have lessened this liability, that surgical treatment is often too long delayed, and that ulcerative colitis, despite periods of remission and improvement under therapy, is still a relentless disease at present incurable by medical means.

When the disease progresses so that a patient is of very little value to himself or his family, Jones[4] feels that it is obvious he should be operated upon, and that it is a mistake to wait longer hoping that the tide will turn since it will not turn.

Speaking for the Lahey Clinic, Cattell[5] states that formerly approximately 30 per cent of their patients having ulcerative colitis were operated upon. However, as these patients were followed for longer periods of time, up to 10 or 15 years or more, the per-

centage of patients requiring surgical intervention definitely increased. Thus, presently, in a large series of cases surgical intervention was used in approximately 50 per cent of these patients.

Karlson and Dennis,[6] emphasize that the risk of carcinoma is greater than the operative risk in ulcerative colitis of more than five years standing. In a series of 263 cases, 8.3 per cent of those having disease for over five years developed carcinoma, 12.6 per cent of those with disease of 10 years, and 20 per cent of those with disease of 20 years duration developed malignancy. They feel, therefore, that chronic ulcerative colitis of more than five years duration is itself an indication for surgical treatment.

Improvements in technic of ileostomy and care have without a doubt lessened this deterent to surgery. Much of the credit for recent improvement in technic should go to Turnbull and Crile[7,8] for their work on the surgical maturation of the ileostomy. I will review briefly these problems associated with the ileac stoma and describe a technic of ileostomy which has seemed satisfactory.

Problems of the Ileostomy

What are the problems that have made many reluctant to submit their patients to an ileostomy?[3,7,9-14] The first comprise a group that are directly related to the technic of bringing the terminal ileum through the abdominal wall and anchoring it. These are prolapse, retraction, fistula formation, stricture, obstruction due to angulation or adhesive bands, and gangrene of the ileostomy. The second group of problems pertains to the protection of the skin from the ulcerative effect of the ileal content, and the problem of finding a simple, inconspicuous, nonodorous appliance that will remain in place and can be easily managed by the patient.

The third, and most important set of complications has to do with ileal dysfunction as a result of serosal peritonitis of the exposed ileal segment. We are largely indebted to Turnbull and Crile[7,8] for an understanding of this mechanism. It has been common experience that in the postoperative period following ileostomy, frequently between the fifth and tenth day, there has been intractable diarrhea and severe disturbances of fluid and electrolyte balance as a result. Rather heroic efforts at intravenous therapy have often been necessary to keep pace with the discharge from the ileostomy. At other times, abdominal cramps, anorexia, distention, visible peristalsis and complete cessation of any discharge provide obvious evidence of the presence of obstruction. This may, at times, be mechanical in nature, but we believe Turnbull[8] has correctly postulated that more frequently all of the above symptoms are due to varying degrees of the same process, namely, obstruction, partial or complete, not due to mechanical factors, but to a paralytic ileus of the exposed segment. This results from peritonitis of the serosa of the exposed segment. Others have appreciated this fact and have tried to devise methods of protecting the exposed segment. The suggestion of Black and Thomas[15] that these segments be covered with a skin graft is perfectly logical if such a concept is correct. Unfortunately, this technic has often been disappointing because of late contracture and obstruction.

Maturation of the Ileostomy

The classic ileostomy must progress through certain phases before it begins to function normally. Turnbull[8] refers to this sequence of events as "maturation of the ileostomy." Until maturation is complete varying degrees of dysfunction, that is obstruction, persist. In the course of maturation the infected serosal surface slowly contracts and pulls the free mucosal border down toward the abdominal skin. The spontaneous eversion of the ileostomy takes place over a period of four to six weeks and is nature's way of covering the exposed and infected serosal surface. Turnbull suggested that the same process be carried out surgically. He first advocated, in 1953, doing this on the seventh day. Crile[7] has more recently been performing surgical maturation immediately at the time of colectomy. This process of surgical maturation has been included with other details of technic in the following description of the ileostomy, which seems to us to minimize the several problems enumerated above.

Technic of Ileostomy

The first step is the proper selection of the site for the ileac stoma. This is located in the right lower quadrant. The exact spot is chosen by taking a disc, the size of the ring of what-

ever type bag is to be used later, and placing it so it falls on flat, normal skin and does not approximate bony prominences, umbilicus or any incision. Commonly, this spot will be at the level of McBurney's point about midway between it and the midline. A circle of skin approximately 2.5 cm. in diameter is removed from the center of this area. The dissection is then coned downward through all layers of the abdominal wall. The fascial defect should admit one finger. The second step is the selection of a level for division of the ileum. A point is taken at least six inches proximal to any gross involvement of ileum. The bowel is divided there between clamps and a portion submitted to the pathologist for examination of a frozen section. If there is microscopic evidence of inflammatory involvement a higher level is chosen and reexamined until one free of disease is found. Residual disease in the remaining ileum is one of the causes of failure of surgical therapy. The third step is delivery without tension of 5 or more centimeters of ileum through the abdominal wall. In order to achieve this the ileum and its mesentery must often be freed and relaxing incisions made in the mesentery at right angles to its edge. There is no excuse for leaving the ileostomy under tension to invite later retraction. The division of mesentery of the small bowel requires an appreciation of vascular anatomy in this region. In general, length should be gained in the primary and secondary arcades rather than close to the bowel. Noer[16] has made valuable contributions to knowledge on this subject.

The fourth step is fixation of the ileostomy. Dennis[6] strongly advocates the placing of many silk sutures between ileum and peritoneum, and in his hands no fistulas have resulted. We have preferred to rely on internal and external fixation of the mesentery to the abdominal wall. The portion of ileum above the skin is completely denuded of mesentery and this portion of mesentery is sutured to the fascia. The intramural collateral circulation of the ileum is adequate to maintain considerably more than 5 cm. of viable bowel after completely denuding of the mesentery.

The fifth and most important step is that of immediate surgical maturation of the ileostomy. A circular incision is made about the ileum approximately 2 cm. from the skin level. This incision is carried through the serosa and muscularis layers to the level of the submucosa. A cleavage plane is established between the muscular layers and the submucosa without difficulty. The muscular layers and the serosa are then removed distally leaving a length of viable mucosa and submucosa sufficient to evert and attach to the skin edges. Bleeding points are ligated with 4-0 plain catgut; the mucosal tube is then turned inside out pulling down over the protruding ileostomy a layer of normal mucosa, the edge of which is sutured to the free skin edge about the ileum.

The final step is immediate protection of the skin. Normal, healthy skin is the first requisite for a satisfactory ileostomy. This is present when the ileostomy is formed, it must be protected and preserved beginning immediately at the time of operation. It is negligent to allow ileal content to come in contact with the skin at any time in the postoperative period. A polyethylene bag, such as is used for deep freeze storage, is applied using skin adhesive, with a small hole tailored to fit about the ileac stoma. The skin at the base of the ileostomy is protected with karaya powder. No catheters are used in the ileostomy itself; the ileostomy is not dilated at any time. The bag is attached to a tube leading to a drainage bottle. This temporary bag is changed as necessary during the first seven days. By the seventh to the tenth day it should be possible to fit and use some permanent type appliance.

This technic, which represents a combination of ideas selected from previous authors, has seemed to us to minimize the morbidity associated with ileostomy. Particularly, the period of massive ileal discharge with its attendant problems in protection of the skin, and fluid and electrolyte balance are avoided. The ileostomy, by this technic, is essentially healed, mature and functioning normally by the end of the first week. By avoiding infected serosal surfaces and indwelling tubes, the incidence of fistula formation should also be lessened. The prevention of prolapse will still depend upon adequate fixation of the mesentery or upon sutures placed between the ileum and peritoneum. It is not difficult to protect the skin from ileac discharge beginning immediately at the time of operation and throughout the postoperative period with materials and appliances now available. The

anticipation of problems in emotional adjustment to the ileostomy, particularly with regard to the patient's occupation, marriage, athletics and social life can usually be satisfactorily accomplished by an understanding physician and do not usually require the assistance of a psychiatrist.

Surgical Treatment of Acute Ulcerative Colitis

The usual feeling has been that acute cases were best treated medically. The often dramatic effect of ACTH and cortisone during acute exacerbations is well documented.[4,17,18] If there was an inadequate response to medical therapy, ileostomy has been resorted to as a life-saving procedure. Jones[4] denounces medical procrastination in acute ulcerative colitis. He states that if one operates to save the patient's life, it is a reflection on the medical man who has waited too long and let the patient get into such a dangerous condition,—the decision should have been made before that.

If ileostomy is done under such conditions, many surgeons have felt it should be a simple loop ileostomy preferably under local anesthesia. (Such an ileostomy will require later revision.) The abdomen is not explored and the colon is carefully avoided. It has been taught that peritonitis was likely to follow handling of the diseased colon. The approach of Cave[19] is entirely different. He feels that a patient in this condition is a patient who will sooner or later require surgical treatment, and he advocates colectomy without delay if the patient is seen in the acute stage and does not respond very promptly to medical measures. The change from a stormy, febrile, septic course to normal following removal of the colon is quite impressive. Cave has used colectomy and ileostomy at one stage during acute exacerbation of the disease and has performed nine such procedures without fatality. He believes that immediate removal of the colon at the time of ileostomy in the acute phase is the operation of choice. By doing this it is possible to get rid of the huge infected and edematous colon and the patient's improvement is often dramatic. Crile and Thomas, and others[6,20-22] now believe the mortality rate and morbidity of one-stage ileostomy and colectomy for acute toxic ulcerative colitis is less than that of ileostomy alone or of medical management. They reported, in 1953, 15 patients treated in this manner with two deaths.

If a larger series of cases confirms the presumption that one stage ileostomy and total colectomy can be performed during acute exacerbations of ulcerative colitis with a lower mortality and morbidity than ileostomy alone, it certainly is destined to become the treatment of choice. There is little question that the patient is returned to normal activities more promptly by this than by any other form of management. Until the mortality rate for colectomy under these circumstances is finally established, medical management employing corticosteroids remains the most widely accepted method of treatment. If response is not prompt and adequate, it seems reasonable to advise an early rather than a last resort to surgical therapy.

The Staging and Extent of Surgical Procedures

Few, if any, would hold today that ileostomy alone is a definitive procedure in the management of ulcerative colitis. The consensus is that the entire colon including the rectum should be removed. The usual procedure has been to perform this in three stages: first, ileostomy; second, colectomy; and third, abdominoperineal resection.[23] With somewhat more detailed attention to preparation of the patient, replacement of deficit of blood volume and blood loss, and improvements in technic, it has been possible to enlarge the scope of surgery performed at one stage without increasing the mortality or morbidity. It is rather common practice now to do the ileostomy and colectomy at one stage, followed after a six week to six month interval by abdominoperineal resection. There are numerous reports of ileostomy and total colectomy, including the perineal portion, in one stage.[20,22,24,25]

Our preference at the moment is for ileostomy and colectomy in one stage, with abdominoperineal resection following after an interval of six weeks or more. During this period the patient will often regain his normal weight and nutritional status. It seems desirable to remove a large portion of the diseased bowel at the time of the initial procedure. On the other hand, to include abdominoperineal resection with its additional time and blood loss seems to impose some-

what upon the reserve of a depleted and often seriously ill patient.

Failure to remove the rectal segment has often permitted the development of carcinoma of the rectum. This has led to the dictum that the rectum should always be removed when surgical treatment of ulcerative colitis is undertaken. McKittrick[26] braces himself somewhat against this current of opinion and says that he is still not convinced, and in his own practice does not follow the dictate that having done an ileostomy he must go on to total colectomy. He admits that any colon and any rectum which shows active inflammation should be eliminated immediately. However, he reports that he has some young men and women under observation who have normal appearing rectums following subtotal colectomy and in whom he intends to defer abdominoperineal resection. He points out that sexual impotency is quite an additional price for a young man to pay just to be sure he may not get cancer of the rectum 15 years hence. Cattell[5] voices the majority opinion and recommends that when colectomy is necessary for ulcerative colitis, the subsequent procedure of abdominoperineal resection must be done. He further denounces the practice of re-anastomosis of the ileum to the rectum in the false hope that complete remission of the disease in the rectal segment can occur after an appreciable interval. It is his belief that any procedure of this sort is unwise and doomed to failure. Incidentally, it *is* possible to perform perineal resection for *benign* disease without loss of sexual potency.

The consensus is that the total colon, including the rectal segment, should be removed and the trend has been to include the whole of this resection in one stage. Several surgeons have found it possible to do this in a small series of patients without increase in mortality or morbidity.

Discussion

A few of the divergent opinions on several aspects of the treatment of ulcerative colitis have been presented. No attempt has been made to arbitrate these controversial points. The real hope in ulcerative colitis lies in research to determine its etiology and thereby bring about effectice preventive or curative medical measures. Meanwhile, as in cancer, surgical treatment, which is really illogical and mutilating, is nonetheless the only hope of cure in many patients. With the advent of several of the newer groups of drugs, hope has recurred that medical cure of ulcerative colitis would now become possible. This has failed to materialize and although much benefit and improvement is derived from medical treatment and prolonged remissions with and without treatment may occur, permanent cure of the disease by any presently known medical management does not seem likely. This is not to say that all, or even most patients with ulcerative colitis should be submitted to operation. It does seem that those patients incapacitated by their disease, those in whom the disease progresses despite medical treatment, those with recurrent, severe, acute exacerbations and certainly those with premalignant changes should be urged to have early surgical treatment. To await the development of severe complications through long periods of debilitation, when the patient could be enjoying an active and relatively normal existence, does not seem justified. Newer technics of producing an ileostomy and care have minimized the complications which have deterred many from this more aggressive surgical approach to the treatment of ulcerative colitis.

Summary

1. The indications for surgical intervention in chronic ulcerative colitis have been reviewed.

2. Complications of the ileostomy have been discussed.

3. A technic of ileostomy including surgical maturation has been described.

4. The role of surgery in acute, fulminating ulcerative colitis has been discussed with reference to the one-stage total colectomy and ileostomy during the acute episode.

5. The staging and extent of surgical resection in ulcerative colitis are discussed.

6. The lack of knowledge concerning the etiology of ulcerative colitis, the limitations of medical therapy, and the complications of surgical treatment are reflected in the many divergent opinions that prevail concerning these problems.

References

1. Grace, W. J., Pinsky, Ruth H., and Wolff, H. G.: The Treatment of Ulcerative Colitis, Gastroenterology 26:462, 1954.
2. Susnow, D. A.: Isoniazid Therapy in Chronic Ulcerative Colitis, California Med. 81:67, 1954.
3. Bargen, J. A.: The Ileac Stoma for Ulcerative Colitis (editorial), Gastroenterology 27:491, 1954.

4. Jones, C. M.: Medical Management of Ulcerative Colitis, Am. J. Surg. 86:608, 1953.
5. Cattell, R. B.: Surgical Aspects of Chronic Ulcerative Colitis, Am. J. Surg. 86:613, 1953.
6. Karlson, K. E., and Dennis, C.: The Elimination of Postoperative Morbidity in the Surgical Management of Chronic Idiopathic Ulcerative Colitis, Am. J. Gastroent. 24:436, 1955.
7. Crile, George, and Turnbull, R. B.: The Mechanism and Prevention of Ileostomy Dysfunction, Ann. Surg. 140:450, 1954.
8. Turnbull, R. B.: Management of the Ileostomy, Am. J. Surg. 86:617, 1953.
9. Brooke, B. N.: The Management of an Ileostomy—Including its Complications, Lancet 2:102, 1952.
10. Colcock, B. P.: Technique of Ileostomy, S. Clin. North America 31:775, 1951.
11. Lichtenstein, I. L., and Herzikoff, S. S.: Recurrent Ileostomy Prolapse—An Old Problem, Ann. Surg. 141:95, 1955.
12. Lyons, A. S., and Garlock, J. H.: The Complications of Ileostomy, Surgery 36:784, 1954.
13. Rogers, A. G., Bargen, J. A., and Black, B. M.: Chronic Ulcerative Colitis: Early and Late Experiences of 124 Patients with Ileac Stomas, Gastroenterology 27:383, 1954.
14. Warren, R., and McKittrick, L. S.: Ileostomy for Ulcerative Colitis: Technique, Complications and Management, Surg. Gynec. & Obst. 93:555, 1951.
15. Black, B. M., and Thomas, J. F.: Skin-grafted Ileac Stoma, Proc. Staff Meet. Mayo Clin. 22:508, 1947.
16. Noer, R. J., and Deer, J. W.: Revascularization Following Experimental Mesenteric Vascular Occlusion, Arch. Surg. 58:1, 1949.
17. Elliott, J. M., and Giansiracusa, J. E.: ACTH and Cortisone in the Treatment of Ulcerative Colitis, New England J. Med. 250:969, 1954.
18. Kirsner, J. B., and Palmer, W. L.: Ulcerative Colitis: Therapeutic Effects of Corticotropin and Cortisone in 120 Patients, Ann. Int. Med. 41:232, 1954.
19. Cave, Henry W.: Personal Communication, 1955.
20. Crile, George, Jr.: The Treatment of Chronic Ulcerative Colitis, Gastroenterology 23:533, 1953.
21. Crile, George, Jr., and Thomas, C. Y., Jr.: The Treatment of Acute Toxic Ulcerative Colitis by Ileostomy and Simultaneous Colectomy, Gastroenterology 19:58, 1951.
22. Ravitch, Mark M., and Handelman, J. C.: One Stage Resection of Entire Colon and Rectum for Ulcerative Colitis and Polypoid Adenomatosis, Bull. Johns Hopkins Hosp. 88:58, 1951.
23. Cattell, R. B., and Colcock, B. G.: The Surgical Treatment of Ulcerative Colitis, Postgrad. Med. 17:114, 1955.
24. Bacon, E. H., and Trimpi, H. D.: Surgical Management of Ulcerative Colitis, J.A.M.A. 153:1249, 1954.
25. Ravitch, M. M.: Total Colectomy in One Stage, S. Clin. North America p. 509, 1954.
26. McKittrick, L. S.: Discussion of Symposium of Chronic Ulcerative Colitis, Am. J. Surg. 86:625, 1953.

Discussion (Abstract)

Dr. George L. Jordan, Jr., Houston, Tex. I wish to compliment Dr. Hagan on his excellent presentation of this problem and to express my appreciation for the privilege of discussing this paper. The need for surgical intervention when complications of ulcerative colitis occur, such as obstruction or perforation, has never been seriously questioned. Also, Dr. Hagan's statement that operation should be performed when the disease progresses so that the patient is of very little value to himself, his family, or the community, would meet with little opposition. The difficulty arises in deciding when that point has been reached. How many attacks must the patient have, and how severe must they be before it can be determined that the disease is not responding to conservative therapy? There are no hard and fast rules which may be followed. The problem must be an individual one for each patient and operation advised when the disability from the disease significantly outweighs the undesirable features of an ileostomy. In planning resection for this disease it is important that the problem of the ileostomy be discussed in detail with the patient before surgical treatment is undertaken, and that he understands the care and management of the ileostomy prior to operation. If the patient is properly prepared for his postoperative course in this manner, many difficulties which can arise in the postoperative period may be minimized.

There is no doubt that difficulties may arise following establishment of an ileostomy. The magnitude of these problems are well illustrated in an article published by Rogers, Bargen and Black approximately a year ago. They studied 124 patients with ileac stomas and found that 86 per cent of patients surviving longer than one year had some type of complication, and that in 43 per cent revision of the stoma was required.

In the past three months we have had to revise three ileostomies because of obstruction. In one case this was due to a twist of the ileum as it came through the abdominal wall, while in the other two it resulted from the more common complication of stenosis of the stoma. One of the latter patients has had virtually all of the complications which may be associated with this operation, including prolapse, retraction, fistula formation, and stenosis. His first ileostomy was performed in 1948 and since that time he has had seven revisions of his ileostomy, or approximately one per year. Four of these were of the conventional type; two were skin grafted ileostomies, both of which stenosed; and the last revision, done only about three months ago, utilized the technic described today. Thus far, function has been satisfactory. This technic has also been used in one additional patient since that time.

The concept developed by Turnbull and Crile is certainly an intriguing one and provides a logical explanation for many of the undesirable sequelae which complicate the establishment of an ileostomy. It is to be hoped that the passage of time and the increased use of this procedure will confirm the early observations so that in the future we may be able to substantially reduce the incidence of stomal complications.

Dr. Gordon McHardy, New Orleans, La. I do not think that we internists can accept as casual an attitude on the surgical attack on ulcerative colitis. While I do agree that Dr. Bargen has been extremely conservative in his attitude, nevertheless he has successfully demonstrated the reversibility of ulcerative colitis even after it has gone through several phases of each of the complications which have been mentioned.

This, on the other hand, does not distract us from the fact that ileostomy with colectomy as a combined procedure is certainly the selective surgical management in intractability and irreversible complication. In elective surgery, however, the patient needs preoperative as well as postoperative education in the significance and complications to the surgery which is planned.

We cannot look upon the surgical procedure, upon the postsurgical morbidity, nor the disability thereafter as simple, nor can we consider these individuals as having a mechanical corrective procedure answering all of their problems. The patient with ulcerative colitis is a complex emotional person who will most often encounter many problems in his struggle with an ileostomy. The emotional contributions to in-

tractability and complications in ulcerative colitis may sustain the patient in illness related to dysfunction of ileostomy.

I consider it imperative that we select surgeons capable of properly investigating that portion of the ileum used for the ileostomy. Too often, we have patients referred to us who had an ileocolitis and the ileostomy was performed with diseased ileum. To stress just how important the problems of these ileostomy patients are has been the creation in the East of an ileostomy club. The ileostomy club may serve the same purpose as Alcoholics Anonymous. The trials and tribulations of ileostomy may seem less significant in a group psychologic approach.

In conclusion, as Bargen emphasized, we must be careful in individualizing those patients who need extensive surgical treatment. Let us educate these patients preoperatively as to their outlook.

Dr. Hagan (Closing). It has been a pleasure to appear on this program, and I would like to thank the discussers for their comments.

We have tried in this paper to give you a sampling of opinions about the treatment of ulcerative colitis. It is obvious that when as much difference of opinion exists, as about ulcerative colitis, there is still a considerable lack of fundamental knowledge. It behooves all of us to do what we can to stimulate interest in research on this problem.

The Postoperative Use of Antibiotics in Anorectal Wounds*

LEON BANOV, JR., M.D.,† *Charleston, S. C.*

It appears that the use of antibiotics adds nothing to the healing of anorectal wounds. The technical aspects of the operation are of far more importance.

THIS IS A PROGRESS REPORT on investigations of the use of antibiotics in proctologic practice. A previous report[1] presented clinical experience with erythromycin and tetracycline in the management of the common nonspecific inflammatory lesions of the anorectum. This report is made to present some of the additional findings to date, to point out the role of photography as an invaluable adjunct in proctologic investigations, and, possibly, to stimulate interest in exploring further the potentialities of antibiotics in lesions of the anorectum.

The full range of usefulness of the broad spectrum antibiotics in proctologic practice has not been fully explored and reported. There have been many reports[2-4] dealing with the antibiotics in the specific infection of lymphogranuloma venereum, some from this clinic.[5-7] Probably because of the difficulties in obtaining and presenting objective evidence, papers[8,9] on the use of the antibiotics in nonspecific inflammatory lesions of the anorectum are few. Moreover, there is a dearth of papers[8] on the use of the antibiotics in postoperative management on anorectal wounds.

In the surgeon's ever continuing search for aids in the healing of wounds, various agents have been tried. Some have been retained; most have been discarded, and even forgotten. The possibility that the newer antibiotics might hasten postoperative wound healing seemed intriguing to this investigator. Since it appeared logical to employ the broad spectrum antibiotics prophylactically to minimize bacterial infection in the heavily contaminated anorectal area and thereby promote wound healing, a study project was set up at the Medical College of South Carolina.

The question posed was,—what is the value of the oral administration of erythromycin and tetracycline in the postoperative management of wounds of the anorectum? This report is an attempt to give an answer.

Method of Study

The clinical material, composed predominantly of private patients, though some ward patients were included, were classified in groups in chance manner. In other words, there was no arbitrary or prearranged way of classifying a case that would "weight" the results. One group of 17 patients received erythromycin, a second group of 14 received tetracycline, and a third group of 16 received no antibiotic and served as a control. Each patient had a history, physical examination, routine blood count and urinalysis. Special chart forms were devised and employed to record the proctologic symptoms and signs in detail.

The operations, all performed by the same operator, included hemorrhoidectomy, fissurectomy, and fistulectomy, either singly or combined. The hemorrhoidectomy was a modified ligature, excision open type. The fissurectomy was a modification of the type described by Gabriel.

Because of the reported low incidence of side reactions, orally administered erythromy-

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This investigation was supported, in part, by grants from Abbott Laboratories; Lederle Laboratories Division, American Cyanamid Company; and Eli Lilly and Company.

The erythromycin used in this study was Erythrocin, trade name of Abbott Laboratories, and Ilotycin, trade name of Eli Lilly and Company, and was supplied by these companies.

The tetracycline used in this study was Achromycin, trade name of Lederle Laboratories Division, American Cyanamid Company, and Tetracyn, trade name of Chas. Pfizer & Co., and was supplied by the former company and J. B. Roerig and Company.

Color slides illustrating cases presented before the Section on Proctology, Southern Medical Association, could not be reproduced for this Journal.

cin and tetracycline were used in this study. The dose schedule used for erythromycin was 400 mg. every 6 hours, for tetracycline, 250 mg. every 6 hours. In all cases the drug was started within 4 hours after operation. In order to insure that the patient received the prescribed medication on schedule, the drug was given postoperatively throughout the remainder of the hospital stay which ranged from 3 to 7 days, four and a half days being the average.

The accompanying table shows the grouping of operations used in this study (Table 1).

Photography was employed in this project to supplement clinical observations and to provide lasting objective evidence of the results. A fixed focus camera, keeping the same distance from image to lens to film, and equipped with electronic flash was used to produce constant uniformity of the pictures. The camera photographed in color the lesion before, immediately after the operation, and at weekly intervals thereafter until healed. The photographs were numbered, mounted in glass, catalogued and filed. These color slides have assisted immeasurably in promoting, to borrow a legal phrase, "a meeting of the minds" for they show the results of the investigation better than words. Moreover, the photographs have provided tangible and valid evidence from which conclusions may be drawn. A camera should be standard equipment for every proctologist.

TABLE 1

CASES STUDIED AND PHOTOGRAPHED

Control	*Erythromycin*	*Tetracycline*
Hemorrhoidectomy	Hemorrhoidectomy	Hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Fissurectomy hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Fissurectomy hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Fissurectomy hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Fissurectomy hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Fissurectomy hemorrhoidectomy
Hemorrhoidectomy	Hemorrhoidectomy	Fissurectomy hemorrhoidectomy
Fissurectomy hemorrhoidectomy	Hemorrhoidectomy	Fissurectomy hemorrhoidectomy
Fissurectomy hemorrhoidectomy	Fissurectomy hemorrhoidectomy	Fissurectomy
Fissurectomy hemorrhoidectomy	Fissurectomy hemorrhoidectomy	Fistulectomy
Fissurectomy	Fissurectomy hemorrhoidectomy	Fistulectomy hemorrhoidectomy
Fissurectomy	Fissurectomy hemorrhoidectomy	
Fissurectomy	Fissurectomy hemorrhoidectomy	
	Fistulectomy	

In analyzing the cases for this study, the charts were reviewed and the color slides were shown in sequence on the screen. Repeated showings of the color slides facilitated comparison of the cases in each group.

Results

Careful study and comparison of the cases in the three groups showed no significant variations. There was no discernible difference in the appearance of the wounds of the three groups when compared at the same postoperative intervals. Moreover, the healing time of the wound was not accelerated by the antibiotics. In addition, the antibiotics did not reduce the need for postoperative narcotic and analgesic medication.

As a group, the patients tolerated the antibiotics very well. Erythromycin had to be stopped in only one patient because of nausea and abdominal pains. Likewise, tetracycline had to be stopped in only one patient because of severe nausea.

It is of interest to note that erythromycin did not prevent the development of a moderately severe grade of cystitis in a patient who required postoperative catheterization. Erythromycin was discontinued after the third day and a triple sulfonamide preparation was used to treat successfully the urinary tract infection.

Incidentally, mention might be made of an experiment to test the observations and reactions of individuals not connected with this investigative project. The color slides were shown to a group of 24 junior medical students on the surgical service. The test was explained to the students. Slides of five cases from the control group were shown to provide a basis for comparison. Next, the slides of 20 cases selected at random from this study, some from each of the three groups, were presented. After seeing the slides, the students decided and recorded their impressions as to whether the case received erythromycin or tetracycline or no drug.

The students' observations were reviewed and tabulated. From a showing of the photographs the students could not select which cases received a drug and which cases received none. In computing the statistics, a majority

opinion was correct in only 12 out of the 20 cases presented. This seems to be a poor percentage considering that the factor of guessing by the student was not eliminated. This presentation of color slides to the medical students effectively pointed out that there was no demonstrable evidence of value of erythromycin and tetracycline in the dosages used to improve postoperative anorectal wound healing.

Discussion

In this study of the use of antibiotics in anorectal wound healing, the number of cases is relatively few. However, the cases have been carefully studied and the healing lesions photographed at periodic intervals. The color slides, studied and compared with a control group, gave excellent objective evidence and provide valid results. A larger series of cases reflecting a greater variety would be statistically more significant.

Considering the dosages, perhaps, an insufficient dosage for too short a period of time could account for the lack of effectiveness of the drugs in producing demonstrable superior anorectal wound healing. Some questions that can be raised for future studies are: Might the same dosage over a longer period of time improve wound healing? Had the drug been started a day or several days preoperatively and continued for a longer period, would the results be more satisfactory? Should a larger dose schedule be used? These and other questions await future studies.

Anorectal wound healing is in great measure dependent upon some other factor than antibiotics. While there are other factors involved in pre- and postoperative care, it is still the operation itself which plays the dominant role in influencing healing of the wound. The antibiotics in the dosages used appeared to have a negligible effect on the postoperative course of the cases studied.

The color slides, forming the tangible evidence of the investigation, can be re-examined repeatedly to permit comparison. Moreover, the color slides increase the validity of the investigation because they supply objective evidence. In proctologic and other research projects, it is difficult to subordinate the human equation. However, photographs supply the proof and the support for the results as well as the conclusions. As an ideal goal for which to strive, daily photographs of the healing process might be considered in future studies. This would, however, add to the costs of investigation.

Conclusion

Neither erythromycin 400 mg. every 6 hours, nor tetracycline 250 mg. every 6 hours administered orally for three to seven days significantly promoted postoperative wound healing of the anorectum.

Photography proved an invaluable aid in proctologic investigations.

Further studies on the use of antibiotics in anorectal lesions are indicated.

References

1. Banov, L., Jr.: Antibiotics in Anorectal Lesions. Antibiotics Annual (1954-55), New York, Medical Encyclopedia, Inc., 1955, pp. 263-268.
2. Wright, L. T., Sanders, M., Logan, M. A., Prigot, A., and Hill, L. M.: Aureomycin: A New Antibiotic with Virucidal Properties. I. A Preliminary Report on Successful Treatment in Twenty-Five Cases of Lymphogranuloma Venereum, J.A.M.A. 138:408, 1948.
3. Rowe, R. J.: Evaluation of Chloromycetin as an Adjunct to the Surgical Management of Lymphogranuloma Venereum and Segmental Ulcerative Colitis, Am. J. Surg. 81:42, 1951.
4. Fletcher, A., Sigel, M. M., and Zintel, H. A.: Aureomycin Therapy in Lymphogranuloma Venereum, Arch. Surg. 62:239, 1951.
5. Banov, L., Jr.: The Newer Antibiotics in the Treatment of Rectal Strictures of Lymphogranuloma Venereum, South. M. J. 46:269, 1953.
6. Banov, L., Jr.: Rectal Strictures of Lymphogranuloma Venereum: Some Observations from a Five-Year Study of Treatment with the Broad Spectrum Antibiotics, Am. J. Surg. 88:761, 1954.
7. Banov, L., Jr., and Goldberg, J.: Erythromycin Treatment of Lymphogranuloma Venereum. Antibiotics Annual (1953-54), New York, Medical Encyclopedia, Inc., 1953, pp. 475-479.
8. Boling, E., and Finch, H.: Results of Use of Chloramphenicol and Other Antibiotics in Proctologic Practice, South. M. J. 45:354, 1952.
9. Banov, L., Jr.: Painful and Painless Anorectal Lesions, J. South Carolina M. A. 48:8, 1952.

Discussion (Abstract)

Dr. John Q. McGivney, Galveston, Tex. I find myself in very little disagreement with what Dr. Banov has said. I would like to congratulate him on the thoroughness of his investigation and the integrity of his results.

I am sure that most of us have had scientific-minded patients and colleagues inquire about the use of antibiotics in anorectal surgery. Until recently, we had only a limited amount of investigative work upon which to base our opinions. But now, Dr. Banov has given us graphic evidence from which we may draw our own conclusions.

Our experience in the use of broad spectrum antibiotics for anorectal surgery, has been similar to Dr. Banov's. As a matter of fact we have, on a number of occasions, sterilized the bowel with neomycin and Sulfathalidine for anorectal procedures only to find that our wounds differed very little in appearance and healing time from the controls.

I am afraid that one who takes it upon himself to manipulate the flora of the bowel for his own purposes soon finds himself in great difficulty. There is an old French proverb which reads "there are no diseases, just sick people;" and it would be well for us to remember this in treating patients with antibiotics. I am afraid that we often fall into the habit of treating bacteria rather than people. It would be well for us to weigh the advantages of the antibiotics against the consequences of their side effects and in doing so, one must not confuse the problems of large bowel surgery with those of anorectal surgery. In the former, one must make certain to avoid infection otherwise disastrous consequences may result, and therefore one is justified in taking a calculated risk. In the latter, flat, well-drained anorectal wounds should invite only a small amount of surface infection and this should be easy to contain by such simple methods as cleanliness and heat. If suppuration occurs, it should be easy to treat it by incision and drainage since it is readily accessible.

It is obvious then that the hazards of the side effects of the broad spectrum antibiotics are of much more consequence than any infection that may involve an anorectal wound. This is especially true when the absorbable drugs are used, since they are much more selective in their action and are absorbed into the general circulation. However, even the poorly absorbed antibiotics and sulfonamides have their disadvantages since they are irritating to anorectal wounds. It is important for us to remember that no matter what the purpose for the use of the antibiotic, it has a profound effect upon the flora of the bowel, thereby upsetting the natural balance and symbiosis which is so important to maintain.

Ultimately we are forced to admit that the use of antibiotics in anorectal surgery is impractical since we have little to gain and much to lose. We must therefore convince our colleagues that the use of antibiotics in anorectal surgery is not only impractical but dangerous. Even the topical use of these drugs is not advisable since this may sensitize the patient to a drug which later on may be of life-saving importance to him. Sound surgical principles and refinements in surgical technic are still the greatest boon to the anorectal surgeon. This includes the creation of flat well-drained surgical wounds, the use of a minimum of suture material and the abandonment of mutilative technics such as the amputative and flap methods of hemorrhoidectomy.

The topical use of a drug low in sensitivity index, such as Furacin, or an antibiotic not often used orally or parenterally such as Polycin is not objectionable and often facilitates healing. We are at present conducting an investigation to determine the value of topical hydrocortisone on anorectal surgical wounds, but at the present time our results are inconclusive.

Dr. Mark M. Marks, Kansas City, Mo. I was glad to hear Dr. Banov's paper because it deals with fundamentals and is of interest to all who are concerned with wound healing. In a study on the effects of cod liver oil in proctologic wounds I found that when physiologic balance in the individual was correct, his injuries would be repaired at a specific rate. The primary function of the surgeon was to assist wherever he could.

Hemifacial Spasm*

MILES L. LEWIS, JR., M.D.,† *New Orleans, La.*

This is a disease to be differentiated from facial tic. Though its cause is unknown, treatment consists of a surgical attack on the seventh nerve.

WHEN AN OTOLARYNGOLOGIST CONSIDERS DISORDERS OF THE FACIAL NERVE, it is understandable that peripheral facial paralysis, either spontaneous (Bell's palsy) or traumatic, comes to mind first. He is likely to disregard hemifacial spasm or, if he considers it at all, to confuse it with facial tics and think that he has no place in its evaluation or treatment. If he has had the experience of caring for a patient with hemifacial spasm, he realizes the great misfortune of these people and faces the frustration of their management.

Hemifacial spasm is an organic disease of the facial nerve,[1] a distinct clinical entity to be differentiated from facial tics and other spasms of the head and neck. Williams, Lambert and Woltman[2] pointed out the following differential characteristics of hemifacial spasm: (1) there is intermittent twitching of the facial muscles; (2) the eyelids are always involved; (3) the condition is almost always unilateral; (4) it occurs during sleep; (5) there is no compulsion to perform the movement and no satisfaction in its performance; (6) the patient cannot control or suppress the spasms and cannot produce them at will; (7) psychic upsets and voluntary facial movements often make the spasm worse; (8) children do not have hemifacial spasm; and (9) only muscles innervated by the facial nerve are affected.

Hemifacial spasm is unusual but not rare. Ehni[3] studied 600 patients with pathologic facial movements, 106 of whom had hemifacial spasm. In his series women predominated in a ratio of 6 to 4 and there were no children.

Etiology

The cause of hemifacial spasm is in doubt but it is definitely believed to be a lesion of the lower motor neuron. The similarity of cryptogenic hemifacial spasm and hemifacial spasm secondary to peripheral facial paralysis has been studied extensively.[1,4,5] It was this similarity, as well as other associated phenomena (weakness, synkinesis, contracture), which first directed attention to the possibility that hemifacial spasm might be a lesion of the lower motor neuron and indeed similar to Bell's palsy. Woltman and Ehni[6] had a patient whose hemifacial spasm was unaltered by a stroke. Duel[4] noticed no change in the spasm in monkeys whose Rolandic cortex had been removed after hemifacial spasm had been developed by section of the nerve and resuture. Fowler[5] failed to note any change in the facial motor cortex in monkeys with hemifacial spasm.

Wartenberg,[1] who has studied hemifacial spasm extensively, theorized: "The facial nucleus contains two motor systems analagous to the pyramidal and peripheral nervous systems and that like these systems a lesion of the upper produces hemifacial spasm (or spastic paralysis) and the lower Bell's palsy (or flaccid paralysis)." He thought that this nuclear lesion might be infectious, degenerative or an inferior anlage. He believed that in facial paralysis both systems are involved and that when recovery occurs, the lower, phylogenetically older system, recovers first and more completely; hence hemifacial spasm develops secondary to facial paralysis.

Williams and co-workers[2] who considered cryptogenic hemifacial spasm to be a lesion of the lower motor neuron, decompressed and performed neurolysis on the vertical portion of the nerve in the mastoid. They were surprised that the synkinesis exhibited by these patients disappeared postoperatively. This is in complete conflict with the generally accepted idea that synkinesis is due to a branching of the axons which are distributed to widely separated muscle groups and suggested to them that synkinesis is due to a reversible physiologic mechanism rather than an irreversible anatomic one. They suggested

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that cross firing of impulses from one nerve fiber to another in a damaged area of the nerve in the facial canal produced synkinesis. They believed that the level at which this occurs is at, or just above, the stylomastoid foramen.

There are isolated cases in which hemifacial spasm has been produced by lesions at the cerebellopontine angle as the result of pressure on the nerve trunk.[7] Thus, hemifacial spasm may be classified as: (1) primary (cryptogenic, idiopathic), or (2) secondary (postparalytic) following Bell's palsy, traumatic facial paralysis, or lesions of the nerve between the pons and the internal auditory meatus.

Treatment

Hemifacial spasm is a chronic progressive illness with only rare spontaneous remissions. Treatment has been fraught with poor results, temporary relief, facial paralysis and disappointment. Alcoholic injection of the offending branches affords only temporary relief. Selective section of the branches to involved muscles distal to the parotid gland substitutes paralysis for spasm and frequently is temporary because the fibers regenerate. Anastomosis of the distal end of the seventh nerve with the proximal end of the eleventh[8] relieves the spasm but adds lack of emotional response and annoying associated movements.

German,[9] in 1942, partially divided the offending branches, stripping them back and ligating the cut portion with some success. Williams and associates,[2] who decompressed and did neurolysis on the vertical portion of the nerve in the temporal bone in 9 patients with cryptogenic hemifacial spasm, found evidence of compression of the nerve at or just above the stylomastoid foramen in four. They reported good results in three, a fair result in one and poor or only temporary relief after two years in five. Kettel[10] performed a similar procedure on 11 patients earlier, but published his experience later in the light of the report of Williams and co-workers. The nerve was normal in six of his patients and showed minor abnormalities near the stylomastoid foramen in five. One of the 11 patients was cured, fair results were obtained in four, and only temporary relief was obtained in six. Kettel thought that the pathologic process is in this region, but that in his patients by the time decompression was performed, irreparable change had occurred in the nerve.

The most encouraging recent report on the surgical treatment of hemifacial spasm is Scoville's.[11] Under local anesthesia he exposed the nerve just distal to the stylomastoid foramen and sectioned two-thirds of the nerve at this point, stripped back the sectioned segment and sutured it to the sternocleidomastoid muscle. He reported one perfect, one poor and four good results in six patients followed for two years. In no patient was there permanent paralysis of any facial muscle.

I have done decompression and neurolysis of the facial nerve from the horizontal canal to the stylomastoid foramen on three patients with cryptogenic hemifacial spasm, with complete relief for three months, then a full return of the spasm in one, complete relief for several months and then partial return of the spasm in another, and complete relief of the spasm for over a year in the third. No abnormality of the nerve was noted in any of these patients. Facial paralysis did not develop after decompression.

In the light of Scoville's report,[11] which indicates that the nerve fibers are not oriented at the level of the stylomastoid foramen, it has occurred to me that it might be desirable to follow decompression and neurolysis of the vertical portion of the nerve with a procedure similar to Scoville's in the mastoid region. The nerve could be sectioned one-half to two-thirds of the way through, then both cut segments of the nerve be stripped back and buried in holes drilled in the dense bone just posterior to the fallopian canal, and be sealed there with bone wax to prevent regeneration of the divided fibers. This could be done rather easily as a secondary procedure if spasm were not relieved by decompression alone. Unfortunately, the opportunity to try this technic has not yet presented itself.

Summary

Hemifacial spasm is an organic disease of the facial nerve. It should be differentiated from habit spasms and tics of the head and neck which involve muscles other than those supplied by the facial nerve, are often bilateral and may be controlled at will. Psychiatric and other nonsurgical measures do not materially affect hemifacial spasm, and until this

distressing condition is more clearly understood, partial section of the main trunk of the facial nerve appears to be the treatment of choice.

References

1. Wartenberg, Robert: Hemifacial Spasm, New York, Oxford University Press, 1952.
2. Williams, H. L., Lambert, E. H., and Woltman, H. W.: The Problem of Synkinesis and Contracture in Cases of Hemifacial Spasm and Bell's Palsy, Ann. Otol. Rhin. & Laryng. 61:850, 1952.
3. Ehni, George: Facial Twitching, Proc. Staff Meet. Mayo Clin. 19:129, 1944.
4. Duel, A. B.: Study of Muscle Spasm Occurring During Recovery from Facial Palsy, Tr. Am. Laryng. Rhin. & Otol. Soc. 23:224, 1933.
5. Fowler, E. P., Jr.: Abnormal Movements Following Injury to the Facial Nerve, J.A.M.A. 113:1003, 1939.
6. Ehni, George, and Woltman, H. W.: Hemifacial Spasm, Arch. Neurol. & Psychiat. 53:205, 1945.
7. Campbell, E. H., and Keedy, C.: Hemifacial Spasm: A Note on the Etiology in 2 Cases, J. Neurosurg. 4:342, 1947.
8. Adson, A. W.: Neurosurgical Treatment of Muscular Spasms and Spastic Painful and Trophic Lesions of the Extremities, S. Clin. North America 13:895, 1933.
9. German, W. J.: Surgical Treatment of Spasmodic Facial Tic, Surgery 11:912, 1942.
10. Kettel, Karsten: Decompression of the Facial Nerve in Cases of Hemifacial Spasm, Danish Med. Bull. 2:56, 1955.
11. Scoville, W. B.: Partial Section of Proximal Seventh Nerve Trunk for Facial Spasm, Surg. Gynec. & Obst. 101:495, 1955.

Recent Developments in Public Health Training for Civil Defense*

EDGAR B. JOHNWICK, M.D.,† *Atlanta, Ga.*

The author outlines the public health problems which would appear as an aftermath of a thermonuclear bomb. The organization of Public Health personnel integrated with the available trained civilian persons is described.

NEW DISCOVERIES ADDED TO THE OLD now make it possible to save more lives than ever before. Conversely, the power to destroy life has never been stronger than it is now. Modern war has become the large scale practice of public unhealth.

A thermonuclear bomb is a man-made catastrophe and one of its tactical purposes is to serve as a city-buster. The incidental radioactive fallout from such a bomb will sift downwind over thousands of square miles. Many such bombs exploded in many places in a nation can make large areas hazardous for human life for variable periods of time. Before, during, or after such an attack, a determined and aggressive enemy can also deliver poison chemicals or biologic organisms in quantities sufficient to cause casualties, confusion, and distress.

Today's plan for continued public health activity during a modern war is forecast by three factors: (1) the new environment; (2) the state of society at the time; and (3) the old and new public health problems that may arise.

It is disheartening today to face the tasks envisioned in the aftermath of tomorrow's war. To make workable plans for common public health defenses, the most important assumption is that thermonuclear bombs of certain size will explode in certain localities simultaneously. If this occurs as anticipated, almost everything in the area will be destroyed including:

(1) Those personnel resources that failed to escape.
(2) Record collections and reporting systems.
(3) Communication facilities as we know them now.
(4) Control points for transportation networks.
(5) Vehicles and the fuel to run them.
(6) Generating stations and the gas and electricity they produce.
(7) Hospitals and diagnostic laboratories.
(8) Stores of medical and sanitation supplies.
(9) Food, clothing, and adequate shelter.
(10) Production and repair facilities for necessary equipment.
(11) The monetary system as we know it now.
(12) Other organizations on which reliance was placed in the past.

Public health activities now depend on full complements of urban resources and services, the most important of which are teams of trained people.

A smoothly working, well-practiced shelter and evacuation plan, and a reasonable interval between the signal for alert and the explosion will determine the number of casualties in the target area and the size of the public health problem in the counties. The more successful the evacuation plan, the larger the resultant public health problem.

The mass influx of people into a new environment will create immediate changes and the reorganization of public health services will be required at once. The subsequent discovery of a new danger in the form of communicable diseases may compel a support area with all of its refugees and resources to be evacuated. New areas will then become in-

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creasingly crowded. The continued well-being of a once reasonably healthy community will be jeopardized when its population grows far in excess of the fixed resources of its existing health organization. The community has been called an infected herd; a large enough one can be assumed to contain cases or carriers of every known disease. Epidemics can occur at any time.

It is difficult to predict the states of mind of these refugees and of those who receive them. We can be sure that there will be different degrees of psychic disturbances, and that the manifestations in neither individuals nor in groups will be absolute or permanent. However, in this newly distraught society, thrown into an over-crowded environment, the stage will be set for the explosion of epidemics from internal sources. Although a biologic attack may be added for bad measure, it will not have to come in order to bring about the epidemics which an enemy may wish to produce. No doubt many of the common problems which the remaining public health workers of that era will have to face will include:

(1) *Water and food borne diseases:* Typhoid and paratyphoid fever, salmonellosis, diarrheas and dysenteries, staphylococcus food poisoning, botulism, and possibly cholera.

(2) *Insect borne diseases:* Malaria, dysenteries and diarrheas, typhus, and possibly plague and yellow fever.

(3) *Animal borne diseases:* Brucellosis, rabies, murine typhus, psittacosis, anthrax, tetanus, and possibly plague.

(4) *Air-borne diseases and those spread by close association:* Influenza, common colds, pneumonia, childhood diseases.

(5) *Venereal diseases:* Syphilis, gonorrhea, chancroid, and ophthalmia neonatorum.

(6) *Maternal and child health problems:* Premature births, puerperal fever.

(7) *General problems of personal hygiene:* Lack of laundry and bathing facilities; vermin, scabies, impetigo, ringworm.

(8) *Untoward effects on masses of cases of the chronically ill who now receive reasonably good care because facilities and medication are available:* Diabetes, severe allergies, mild heart disease, etc.

(9) *Radiation sickness in those exposed to single doses of total body radiation:*

(a) Large dose (600r): Nausea and vomiting in 1 to 2 hours, diarrhea, inflammation of nasopharynx, fever, rapid emaciation, death in 1 to 2 weeks. Mortality 100 per cent.

(b) Median dose (400r): Nausea and vomiting in 1 to 2 hours, no symptoms for about two weeks, loss of hair beginning at the end of second week, loss of appetite, malaise, fever, pallor, diarrhea, epistaxis, purpura, emaciation, death in about 4 weeks. Mortality about 50 per cent.

(c) Moderate dose (300 to 100r): No definite symptoms for about two weeks, combinations of possible symptoms including all of those listed under median dose. Recovery likely unless complicated by other injuries or previous poor health or other infections.

(10) *Radiation sickness in those accumulating small increments of radiation over long periods of time:* Effects on the continued health of those exposed; effects on the health of the progeny of those exposed.

(11) *Effects of sublethal doses of radiation on diseases that normally have a low mortality but a high morbidity:* Chickenpox, measles, salmonellosis, common colds, gonorrhea, etc.

The public health problem in civil defense is old in many ways, but a new aspect is the ubiquitous hazard from radioactive bomb wastes, which casts a new perspective on an unprecedented and unaccustomed scale.

The Federal Civil Defense Administration, under its charter from Congress, delegated certain civil defense responsibilities to the Secretary of Health, Education, and Welfare, and the Secretary, in turn, assigned the public health aspects of civil defense to the Public Health Service on August 14, 1954. The Public Health Service has been assigned the function to plan and develop, for use by the States, in coordination with the Federal Civil Defense Administration, and through customary channels, a program concerned with:

(1) The control of hazards to man from biologic and chemical warfare.

(2) The development of public health reserve personnel resources.

(3) The development of measures to minimize injury to personnel and to vital functional components of public health facilities.

(4) The development of plans for emergency restoration of community facilities essential to health.

Public Health Service activities in these areas are supported by funds made available from the Federal Civil Defense Administration appropriations. The Public Health Service, in many of its Divisions, is now carrying out research activities and is conducting a re-

cruitment and orientation program for reserves. One of the Divisions of the Public Health Service, the Communicable Disease Center in Atlanta, is carrying out research in civil defense measures, a training program for active and reserve officers, and a state-directed training program for public health personnel in the states.

The Center began its training activities in September 1954 in cooperation with the Sanitary Engineering Center in Cincinnati. First, a series of eight regional meetings, attended by key representatives from the health departments of all states, was held. The Center is now conducting a series of general civil defense training courses in individual states, with 25 to 40 key members of the state's public health and civil defense staffs in attendance. The courses are about three days in length, depending on the state's needs, and are given jointly with a group of training officers from the Sanitary Engineering Center.

These short courses stress the team approach for the solution of the state's anticipated civil defense public health problems and are intended to be followed by:

(1) A similar or abbreviated course to be presented by the state at the regional, county, or municipal levels, and

(2) Topical training courses for personnel who need specialty training in rapid laboratory diagnostic procedures and other related subjects.

These state courses rely heavily on the teaching resources in the state itself, and one of the purposes is to start these essential training processes in such a way that they may be maintained with as little help from outside of the state as possible. We realize that all states have training resources which, when added together, far exceed those of the Communicable Disease Center and the Sanitary Engineering Center. Our main purpose is to coordinate the existing problems of civil defense with the present resources of public health, and to help assemble a Civil Defense Public Health organization in each state to provide for future emergencies.

In peacetime, help is easily available from many places, some of them distant but accessible. In war, help will have to be sought first locally. Precise action can be taken against a health hazard when it has been identified, and accurate diagnoses in a community will have to be made locally under wartime emergency conditions. However, no action can be taken locally unless there is a trained team ready to act in the field of operations. Effective public health action in time of war will be dependent upon the numbers of small teams made up of self-sufficient people who, with volunteer help, can take independent action promptly and courageously and ask for help later.

The success of civil defense preparedness in public health depends largely upon the initiative, the energy, the imagination, and the independence with which the county and local practitioners of the medical and public health arts can readapt themselves to the anticipated conditions of modern war. With this in mind, the Public Health Service in its training program aims to assist the states both in anticipating diseases and other public health hazards resulting from war, and in training their people for preparedness in wartime emergencies.

Discussion (Abstract)

Dr. Hardy A. Kemp, Houston, Tex. This presentation certainly cannot fail to make a profound impression upon everyone of us, since it is so heavily fraught with dire forebodings. This is a case where we would like to shut our eyes and wish it would go away, and if ever that childhood saying had sincere earnestness, for my part this is it.

The whole picture is so discouraging and so disheartening that it calls upon every ounce of courage we have left not to be too cynical about it, not to be too disheartened, and not just to "plain-flat-out," as we say here in Texas, give up. To give up, of course, would be to deny the heritage of freedom that has been handed down to us through struggle and conflict and victory over all these years.

I am particularly impressed with the simplicity of Dr. Johnwick's outline, which has told us so much in so little. For some of us who are not as close to it or have not studied it as much, it would have taken a great deal more time to say as much as he has, and I doubt if we could have said it as well. He has outlined for us in a clear way what will happen. That, to me, is challenging enough, and I am sure it is to you as well. But I am particularly impressed by the philosophy that his paper expresses, particularly as it appears in the last few sentences of the last few paragraphs. I call your attention once more to the importance of what he has said about *how* and *we will*. With all of our discouragement and with all the attitudes which I personally have and which I hope you do not share, we may still be guided by the simple philosophies that he has expressed. We have first to

realize that, in peacetime, help is easily available from many places. For instance, a minor, even a broad-scope disaster, opens our pocketbooks and our hearts, to which we add our personal services. That is easy in time of peace. In war we are on our own. Those of you who have been in war know what that really means.

He has also pointed out to you that the success of what we in civilian life will do will depend upon initiative and energy and independence and imagination. But the thing that concerns me and I believe those of you too who will have to deal with this problem will wonder from whence will come our authority to act. Shall we depend upon a "natural leader" if he is still alive, and how will we go about that? I trust that that has been given, and I am sure it has been, the most profound consideration in this planning. I have the recollection, and so do many of you, of disorganized retreat and of times when everything seemed to have gone wrong; yet you have the recollection, I dare say, of outstanding people whose natural leadership rose to the occasion. In most instances of that sort it seemed to me that that was because they either had "stripes on their arm" or marks on their helmet indicating some kind of rank for which they had responsibility and for which they had commensurate authority. Surely and undoubtedly our planners will provide some way by which not only we can identify each other, but by the same token the "leaders" who survive will know that they have been given authority along with a tremendous responsibility.

Dr. Johnwick and I had a word or two before the paper was read and I raised the question as to whether a good deal of this should not be directed to the attention of people in the smaller towns and in the outlying centers of our larger cities. We need to attract the attention of our rural county medical societies, not Harris County, or Dallas County, Tarrant, or Bexar County, or some of the rest of our larger ones, but those like the "Ozark Ten Counties" or the "Brewster Seven Counties." We must interest the men there and the women there and the health local organizations there with the type of training outlined here. They will be the ones to care for the survivors.

I hope and trust that all our members read this paper and take it to heart. I thank Dr. Johnwick sincerely for bringing it to us, as I am sure all the rest of our Society will when they get a chance to read it, which they certainly should.

EDITORIALS

POISONING BY IRON

It is probably true that physicians generally have thought of the iron salts as being one of our innocuous drugs. Surely this was accepted until in very recent years. Thus, it was a shock when it was clearly demonstrated less than a decade ago that iron salts were not without danger to young children, and might even result in their death. Strangely this drug was used for generations without any suspicion that it might be toxic to children. There may be two reasons for this. First, fatal poisoning may have masqueraded as the more common infectious diarrheas. Secondly, it is only in more recent years that the iron salts have been coated with attractive green, red and other colored coverings so suggestive of candies, and unaccompanied by the unpleasant taste of the older iron preparations.

The first report of recognized intoxication came from Great Britain, in 1947, by Forbes. In 1950, Thomson[1] reported six instances occurring in five years (1944-1949) from Dundee, having a population of 182,000. Two died and four recovered. Subsequently cases of poisoning have been reported from several countries including a number in this country. Several years ago an editorial[2] appeared in the *Journal of Pediatrics* pointing to the eight fatal cases and to eight nonfatal cases which had been reported up to that time. The same issue of that journal carried two reports on the subject. Since then additional reports have appeared, and therefore the matter may deserve further editorial attention.

From the several reports it appears that most cases have occurred in children from 18 to 30 months of age; thus, no worthwhile history was available. It appears that as few as ten to fifteen 5-grain tablets of ferrous sulphate may be lethal. Since tablets or fragments of tablets have been found in vomitus or the gastric aspirate as late as three hours after ingestion, vomiting makes difficult any accurate approximation of the quantity of iron absorbed. It has been pointed out that the solubility of the enteric coated preparations is variable and that damage to tissue might continue for twenty-four hours.

Davis,[3] in reporting a case of iron intoxication in which recovery occurred, has reviewed the symptomatology and management as did Thomson.[1] Symptoms may appear as early as 30 to 60 minutes after the ingestion of the tablets. Vomiting appears early. There are pallor and drowsiness. Diarrhea followed by dehydration, shock and coma supervene. Hematemesis may occur early, may be severe or occur not at all. The dehydration, shock and acidosis have led to death in about one-half the reported cases. Thomson reported that misleading well-being and playfulness may intervene between the initial symptoms and fatal collapse. Death may occur up to 72 hours after taking the tablets.

The findings at necropsy are edema, hemorrhage, and superficial necrosis of the gastric mucosa, with similar areas and even gangrene in the small bowel. Thrombosed vessels are found in the small bowel. Luongo and Bjornson[4] found hemorrhagic periportal necrosis in the liver.

Treatment includes the use of emetics, gastric lavage, cathartics and enemas. Demulcents and magnesium oxide protect the gastric mucosa. Some recommend the instillation of sodium bicarbonate solution after lavage in the hope of producing an insoluble ferrous carbonate. (BAL seems ineffective.) Fluids, plasma, or blood are used to combat shock.

Prevention is more to the point. Ferrous sulphate should be dispensed and kept in bottles with screw caps,—screwed tightly against prying little fingers. Furthermore, these should be kept on the top shelf. The editorial[2] previously referred to pointed to the hazard of a growing custom of giving donors in blood centers envelopes containing tablets of ferrous sulphate. These and any other containers should carry a warning of the dangers for little children. The doctor has a duty of educating every adult given iron salts of the hazards of the drug to small children.

1. Thomson, James: Ferrous Sulphate Poisoning: Its Incidence, Symptomatology, Treatment and Prevention, Brit. M. J. 1:645, 1950.
2. Editorial: Iron Poisoning, J. Pediat. 40:141, 1952.
3. Davis, David W.: Iron Poisoning, Am. Pract. & Digest Treat. 7:1092, 1956.
4. Luongo, M. A., and Bjornson, S. S.: The Liver in Ferrous Sulphate Poisoning—A Report of Three Cases in Children and Experimental Study, New England J. Med. 251:995, 1954.

THE PURPOSE OF THE MEDICAL EDUCATION

In his address, which appears in this issue, Turner[1] considers the purposes of the medical education. Some of his statements deserve further comment for emphasis, since it appears that in some quarters the purposes of a university medical education either have been lost sight of, or have never been appreciated. These thoughts revolve about whether the undergraduate medical course should be one of education or one of technical training.

Turner objects to glib statements that the objective of a medical school may be expressed as, "to educate physicians for general practice." He objects because of an implication made at times that under such circumstances the basic training "should be something different, something less thorough and exacting than is needed by those who plan to specialize." He emphasizes that there can be no "double standard for basic medical education." His logical assertion then is, "The cultivation and teaching of medicine on a strictly scientific basis is the only sound professional education to offer medical students, regardless of their plans for the future."

It would seem that looking toward the future one might think of *family practice* rather than *general practice*. Under such a definition the training would be basically that of the internist and pediatrician, with knowledge of normal obstetrics and attention to simple emergency surgical management. Turner's thinking makes sense. After all the internist is a "generalist," except for obstetrics and surgery, and surely the problems of daily practice fall in almost all instances into the field of medicine and pediatrics. With good roads and rapid communication, the patient of the complicated obstetric case or the surgical case are within a short time-distance from specialists in hospitals which have all the needed facilities for good care. The family physician with good basic *education* oriented toward internal medicine and pediatrics will know when the specialist is needed. Pickering,[2] in commenting upon training for practice, also points out that the undergraduate curriculum is not for the training of either specialists or general practitioners, indicating that training for either path is dependent upon *graduate* training. He points out that if the *training* of general practitioners were the objective of undergraduate instruction it would appear doubtful that the expense of the preclinical departments could be justified. If *training* only were the objective it would be cheaper not to make medicine a university faculty, but to set up technical colleges offering a smattering of preclinical knowledge and provide clinical training by the old-style apprenticeship.

It can be said probably for most teachers of medicine that they teach with never a thought as to whether the student will be a specialist, general practitioner or an investigator. The teacher's objective is to so train the student that he will be able to collect and evaluate facts related to health and disease. Further, that he have good judgment on health matters affecting the individual and groups. These objectives, if attained, provide a foundation on which the special requirements of either practical or scientific medicine can be built during the graduate training period. By education, in its full definition, the medical student will have been prepared to *learn*, so very important if he is to keep up with, and to evaluate the rapidly advancing thoughts and knowledge of medicine. Pickering quotes Karl Pearson, "The true aim of the teacher should be to impart an appreciation of method rather than a knowledge of facts," pointing out that method outlasts facts. Pickering also quotes Dr. Sidney Burwell as having said, "My students are dismayed when I say to them, 'Half of what you are taught as medical students will in 10 years have been shown to be wrong. And the trouble is, none of your teachers know which half.' "

Thus, it seems most essential to recognize that the purposes of a medical education are not to train a person for an immediate task (or type of practice) but rather to give him the methods, pattern of thinking, and critique to enable him to assimilate and utilize in practice the discoveries of ten or twenty years hence. The training, whether for specialism, general (family) practice, or for a career in research, should be left in the main to the graduate years.

1. Turner, Edward L.: Contributions of Duke University School of Medicine and Duke Hospital, South. M. J. 50:51, 1957.
2. Pickering, G. W.: The Purpose of Medical Education, Brit. M. J. 2:113, 1956.

These thoughts can be summarized by quoting Pickering, "that the function of the medical curriculum is to train the basic doctor, provided that we recognize that the concept of the basic doctor is a mere abstraction." He further suggests, "that the function of university education is to train the student's mind so that he can gather data accurately and so that he can learn to form a balanced judgment on those data."

The Washington Meeting

The Golden Anniversary Meeting of the Southern Medical Association held in Washington, November 12-15, was one of the finest in Southern's 50 year history. It was a fitting climax to the observance of the Association's half century of service to physicians of the South.

The meeting was unique in many ways. First, it was a conjoint effort between the Medical Society of the District of Columbia and the Association. The host Society gave up its regular fall meeting in order to contribute to the scientific excellence and the spirit of the occasion. More than 300 D. C. physicians worked tirelessly for the success of the meeting. In recognition of the host Society's cooperation, Monday, November 12, was designated as "D. C. Day." As a part of Monday's program, two large scientific sessions were conducted exclusively by Washington physicians which attracted capacity audiences. During the Monday evening General Session in the Mayflower, presided over by Dr. Oscar B. Hunter, Jr., Washington, General Chairman, the host Society participated also in the program when Dr. Ralph M. Caulk, the Society's President, gave an address of welcome, the Society's annual awards were presented, and a delightful performance was given by the Washington Doctors' Symphony Orchestra under the baton of Mr. Richard W. Dirksen, Conductor. A photographic review of the celebration of the Golden Anniversary held in Chattanooga, Tennessee, on October 2-3 was also given on Monday night and narrated by Mr. C. P. Loranz. The highlight of the Monday evening session was the President's Address by Dr. W. Raymond McKenzie of Baltimore.

The Scientific Assembly

The scientific program was perhaps the most versatile and diversified in Southern's history. In addition to the splendid D. C. Day sessions, the 20 Sections of the Association held a total of 48 sessions. The second annual Geriatrics Symposium, under the chairmanship of Dr. Milford O. Rouse of Dallas, Texas, along with the scientific sessions of the Potomac and Southern Chapters of the American College of Chest Physicians, the Association for Research in Ophthalmology, Inc., the Southeastern and South Central Regional Committees of the College of American Pathologists, the Southern Gynecological and Obstetrical Society, and the Southern Flying Physicians added further appeal to the scientific assembly. In addition to these formal presentations, panel discussions, symposia, and motion pictures were presented. The members had occasion to visit many of the outstanding medical facilities of the nation's capital, including the National Institutes of Health, the Armed Forces Institute of Pathology, and many of the hospitals and teaching facilities of Washington.

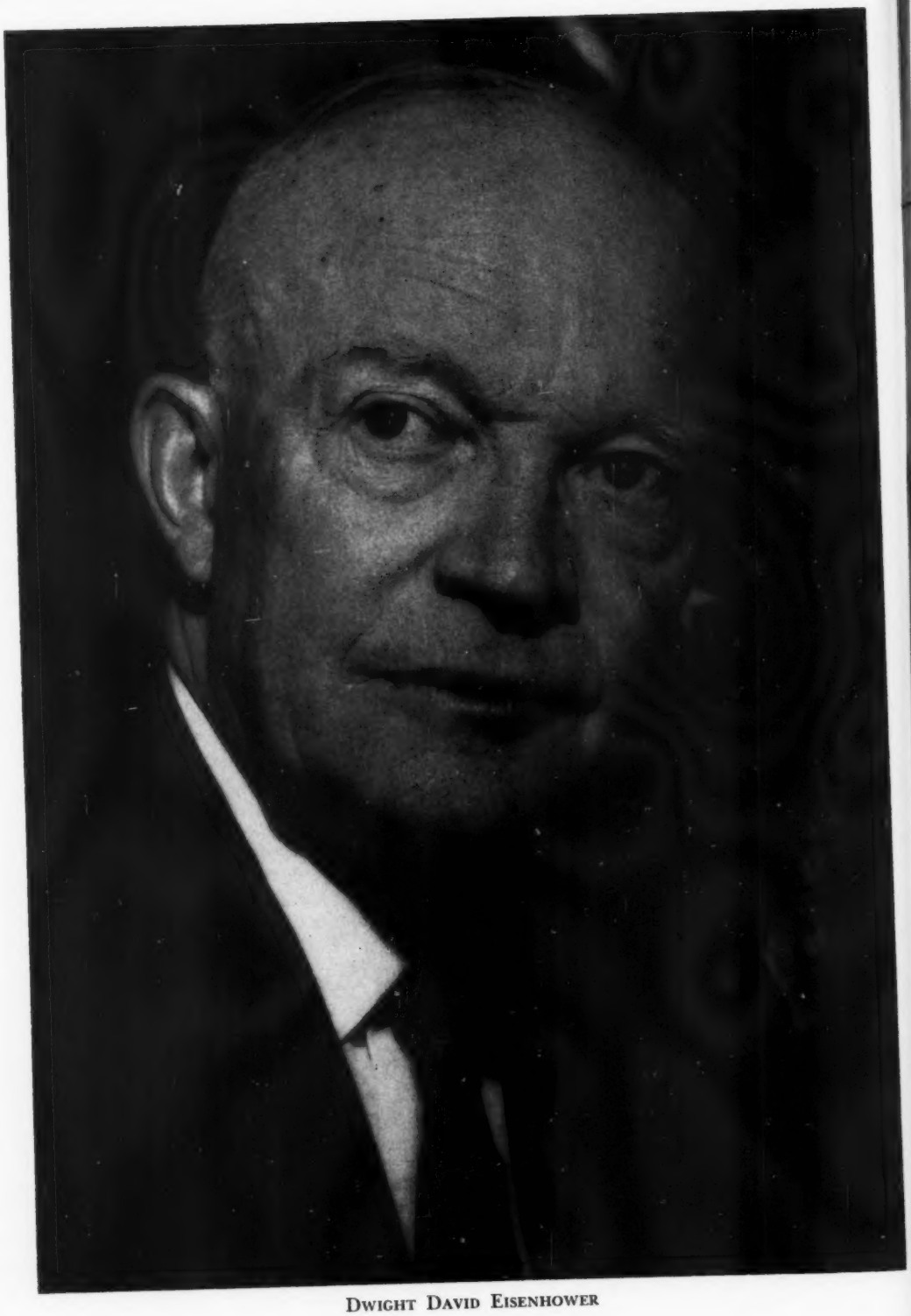
Exhibits

A capacity number of exhibits, both technical and scientific, were housed in the Exhibit Hall and in Sheraton Hall (Ball Room) of the Sheraton-Park. Ninety scientific exhibits and 113 technical (commercial) exhibits were displayed.

Business

The Council of the Association, its policy-making body composed of 17 Councilors from the states within its territory, held two lengthy sessions during the meeting. The

Continued on page 127



DWIGHT DAVID EISENHOWER

President of the United States

THE WHITE HOUSE
WASHINGTON

November 10, 1956

TO THE SOUTHERN MEDICAL ASSOCIATION:

To you who are celebrating the Golden Anniversary of your Association, dedicated to the better health of our people, I send warm congratulations on a record of great achievement.

Certainly, you can look back with pride to the transformation the Southern Medical Association has helped accomplish in all that concerns the well-being, the living conditions, the life expectancy of many million Americans.

As members of the medical profession, setting for yourselves high standards of responsibility and knowledge and zeal, you have demonstrated the dynamic capacity of men and women -- voluntarily joined in cooperative action -- to work for the common good. And, as citizens, concerned with the welfare of homes and communities of the South, you have vindicated our traditional reliance on individual initiative and individual enterprise as the chief source of human progress and betterment.

For the years immediately ahead, we now see unfolding before us new horizons whose attainment will assure all our people increasingly greater assurance of good health and of good care when illness or accident strikes. To the realization of all that these new horizons promise us as a people, I am confident you, the members of the Southern Medical Association, will give untiringly of your energy and knowledge and spirit.

My best wishes are yours for another half-century of achievement.

Dwight D. Eisenhower

W. RAYMOND MCKENZIE, M.D.

Immediate Past President, Southern Medical Association

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BUSINESS MANAGER
C. P. LORANZ
PROFESSIONAL RELATIONS COUNSELOR

November 12, 1956

Dwight D. Eisenhower
President of the United States
The White House
Washington, D. C.

Dear President Eisenhower:

Your letter of good wishes to the physicians of the South during their Golden Anniversary Meeting in the nation's capital this week is greatly appreciated.

As President of the Southern Medical Association, I can assure you that the more than 40,000 physicians in the territory of the Southern Medical Association will continue to render the people of the South the finest medical care.

To the end that our people may continue to enjoy an even better standard of health, all of the professional skills at our command will be used to alleviate illness, allay pain and postpone death.

The physicians of the South, Mr. President, accept your challenge to improve medical care, and they wish to express to you again their deep appreciation for your personal message of good wishes.

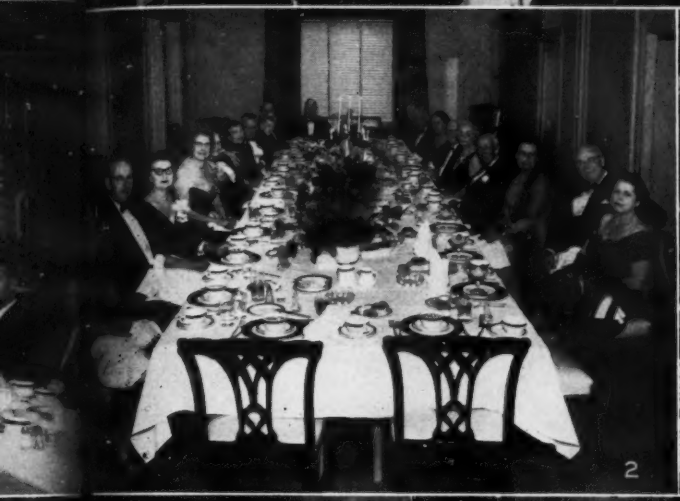
Very truly yours,

W. Raymond McKenzie

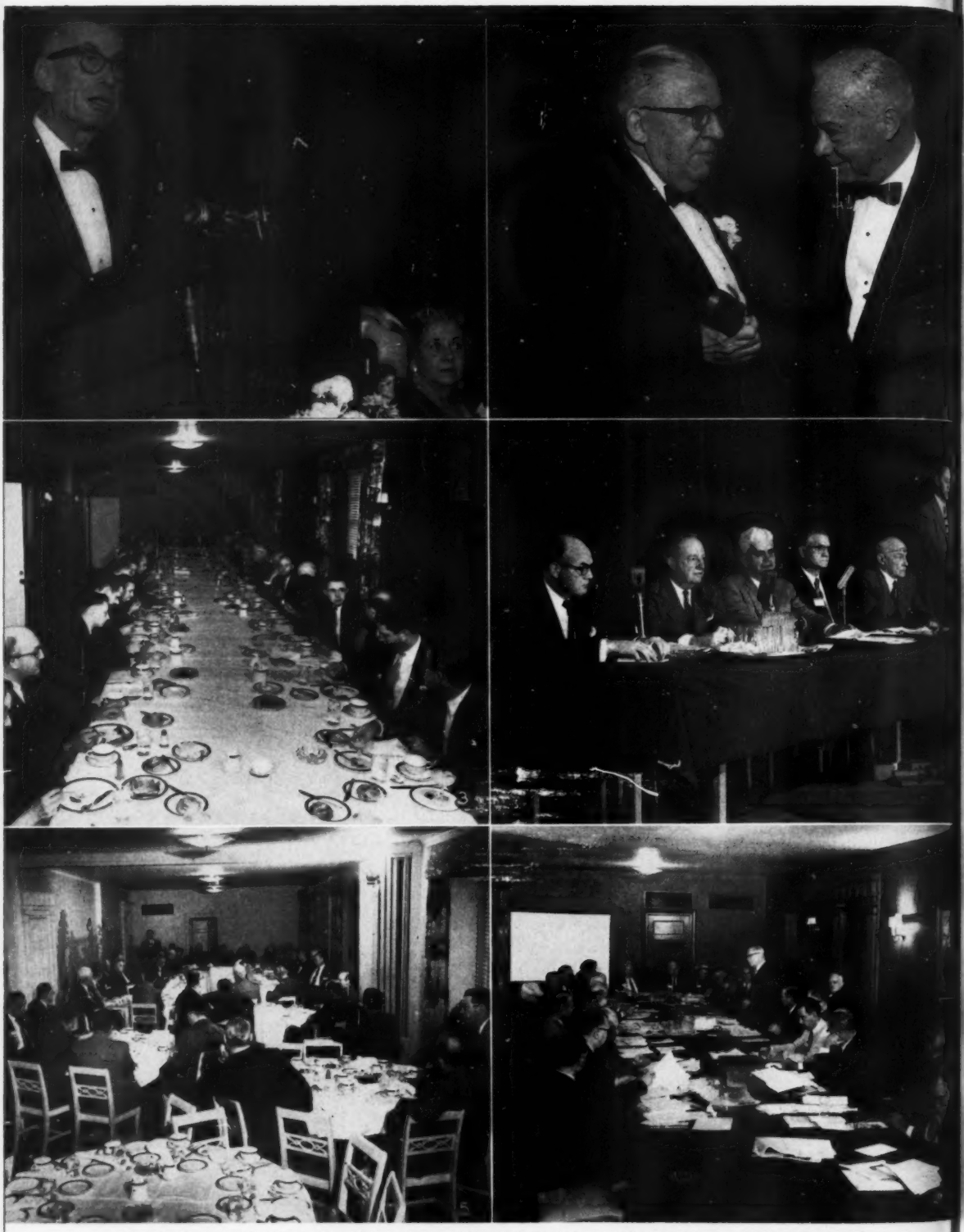
W. Raymond McKenzie, M.D.
President
SOUTHERN MEDICAL ASSOCIATION

WRM:r

(1) Upper left, Registration (2) President-Elect Culpepper and President McKenzie (3) Dinner honoring Medical Student Representatives (5) Student Representatives attend Council Luncheon (6) Dr. Oscar B. Hunter, Jr., General Chairman, presiding at First General Session (Drs. McKenzie and West at Dr. Hunter's right)



(1) (top) Doctor's Day Luncheon, Woman's Auxiliary (2) Past-President's Dinner (3) Mr. C. P. Loranz narrating photographic highlights of Golden Anniversary Celebration held at Chattanooga, October 2-3. Screen located to Mr. Loranz' right. (4) General Session at Mayflower, Washington Doctor's Symphony Orchestra on stage in background.



(1) Dr. David B. Allman, President-Elect, AMA, addresses Second General Session (2) Dr. McKenzie presents gavel to incoming President J. P. Culpepper, Jr. (3) "Meet the Press" Breakfast (4) Typical panel presentation (Industrial Medicine) (5) Joint Council-Section Officer's Breakfast (6) Council in session (Report of Insurance Committee being made by Chairman Grayson Carroll.)

first session of the Council on Saturday, November 10, was preceded by a meeting of the Executive Committee on Friday noon. The Executive Committee heard reports of all officers of the Association and prepared recommendations for the Council's consideration. The Executive Committee also held a Post-Convention session on Thursday morning.

Council Action Highlights

Among the major actions taken by the Council at the Washington meeting were the following:

1. Heard and adopted reports from the Executive Secretary-Treasurer, Business Manager, Advisor and Professional Relations Counselor, and the Editor of the Journal.
2. Adopted the Budget for the fiscal year of 1956-57.
3. Recommended adoption of an amendment to the By-Laws re-establishing the Research Medal and providing for a Committee to recommend nominees as recipients of the Medal.
4. Appropriated a substantial contribution to the Association's Retirement Fund and provided for the administrative costs of the Fund to be paid from the general treasury.
5. Determined the general over-all plan for the Miami Beach (1957) meeting.
6. Authorized the purchase of a lot in Birmingham at the corner of Highland Avenue and 26th Street, South, upon which a modern and adequate headquarters office building will be constructed in the future.
7. Authorized and directed major changes in the Association's Group Sickness and Accident Insurance Program providing for a sliding scale of premium rates based upon age groups and modifying the schedule of benefits.
8. Authorized the continuance of the Medical Student Representatives Program. (Nine medical schools within a 500 mile radius of Washington were represented by elected members of their senior classes. The students were guests of the Association.)
9. Authorized the continuance of the popular Geriatrics Symposium as a special scientific feature.
10. Authorized and directed a Post-Convention Tour to Puerto Rico following the Miami Beach meeting.
11. Authorized and directed the expansion of the Membership Promotion Committees in the various states to include at least one member from each State Medical Society Councilor District.
12. Accepted a joint invitation from the Dallas and Tarrant County Medical Societies to hold an annual session in Dallas with the above Societies acting as joint hosts in either 1960 or 1961. Present schedule of annual meetings is:

    Miami Beach—November 11-14, 1957
    New Orleans—November 3- 6, 1958
    Atlanta —November 9-12, 1959
    Baltimore —November 14-17, 1960

13. Authorized continuing the policy begun this year of paying necessary expenses for one out-of-territory guest speaker for each of the 20 Sections.
14. The following elections were held by the Council: Chairman of the Council, Dr. A. Clayton McCarty, Louisville, Kentucky; Vice-Chairman of the Council, Dr. Fount Richardson, Fayetteville, Arkansas; Member of the Executive Committee, Dr. Harry Lee Claud, Washington, D. C.; Recipient of the first Distinguished Service Award, Dr. Curtice Rosser, Dallas, Texas; Winners of the scientific exhibit awards: first place, Dr. Nicholas C. Hightower, Jr., Dr. A. C. Broders, Jr., Dr. R. D. Haines, Dr. J. F. McKenney and Dr. A. W. Sommer, Temple, Texas; second place, Dr. Garrett Pipkin and Dr. Donald K. Piper, Kansas City, Missouri; third place, Dr. Harwell Wilson, Dr. E. H. Storer and Dr. E. E. Bramlitt, Memphis, Tennessee; re-elected Dr. Lee F. Turlington, Birmingham, Alabama, to a three year term on the Employee's Pension Trust Committee; and elected Dr. W. Raymond McKenzie, Baltimore, Maryland, to the Board of Trustees for a six year term.

Wednesday Evening General Session

The Second General Session, held in the Williamsburg Room of the Mayflower, featured an address by Dr. David B. Allman,

President-Elect of the American Medical Association. His address was followed by a brief report of the Council by Dr. J. Morris Reese of Baltimore and the election of officers. General Officers elected were: Dr. W. Kelly West, Oklahoma City, President-Elect; Dr. Milford O. Rouse, Dallas, Texas, First Vice-President; Dr. Oscar B. Hunter, Jr., Washington, D. C., Second Vice-President. Following the election of officers, Dr. J. P. Culpepper, Jr., Hattiesburg, Mississippi, was installed President by Dr. McKenzie. Closing features of the Wednesday evening session included the presentation of the Past President's Medal to Dr. McKenzie, presentation of first Distinguished Service Award to Dr. Curtice Rosser of Dallas, and announcement of the winners of the scientific awards and the winners of the thirty-third annual golf tournament trophies.

Woman's Auxiliary

The Auxiliary, headquartered at the Mayflower, had a registration of almost 1,000 ladies. In addition to their business sessions, their program featured a most successful Doctor's Day Luncheon on Tuesday in the Ball Room of the Mayflower with more than 200 present. Dr. Louis A. M. Krause of Baltimore, Maryland, was the guest speaker for the occasion. The social side of the Auxiliary was highlighted on Monday, November 12, by a tea and fashion show by Julius Garfinckel & Co. At the close of their sessions, Mrs. O. W. Robinson of Paris, Texas, was installed President of the Auxiliary, succeeding Mrs. John J. O'Connell of St. Louis, Missouri. Local arrangements for the Auxiliary were made under the chairmanship of Mrs. Oscar B. Hunter, Jr. The Auxiliary will hold its thirty-third annual session during the meeting of the Association at Miami Beach, November 11-14, 1957, with headquarters in the Delano Hotel.

Social Highlights

The Washington meeting was typically Southern on the social side. Major events included a reception for the President at the home of Mrs. Oscar B. Hunter, Sr., with Dr. and Mrs. Oscar B. Hunter, Jr., as joint hosts. More than 700 attended. President McKenzie and President-Elect Culpepper were honored by a luncheon on Tuesday by the International Club of Washington. On Wednesday evening, the Association held a reception in the Williamsburg Room of the Mayflower honoring Dr. David B. Allman. Dr. and Mrs. Harry Lee Claud entertained with a reception for the officers of the Association at their home Monday, November 12, at 5:00 p.m. In addition, there were literally dozens of smaller receptions and private parties given by various members of the host Society.

Supplementing the purely social affairs were 19 alumni reunion dinners and parties. Several of the Sections also held luncheons and dinners during the meeting. A feature of the Monday evening programs was a dinner in the Continental Room of the Sheraton-Park honoring the nine medical student representatives.

The Washington meeting was also the largest single meeting in the history of Southern, *both* from the standpoint of physician registration and total attendance. The official count shows 5,438 registrants of which 3,173 were physicians. In addition there were 969 ladies, 314 medical students, and 982 nurses, technicians, exhibitors, visitors and guests.

Thus closed the Golden Anniversary Meeting. The Association, under the leadership of President Culpepper, looks confidently to the fifty-first milestone in the future progress of a unique organization noted for its scientific excellence, its *esprit de corps,* and the friendship and fraternity of its members.

V. O. F.

Fifty Years of Progress*

W. RAYMOND McKENZIE, M.D., *Baltimore, Md.*

TO BE ELECTED PRESIDENT of the second largest general medical association in the United States is a very great honor. To be selected from 10,000 other members for this high position makes the honor even more impressive. To preside at the Golden Anniversary Meeting adds even more honor. For this manifestation of your confidence in me, I am deeply grateful. In addition to the honor, the office carries with it a great responsibility because you, rightfully, should expect your President to further the cause of the Southern Medical Association by crusading for better medicine for all of the people in our territory. I assure you that I have done my best to carry on the work of my predecessors so that the Southern Medical Association will continue to be the best medical association in our country.

The Southern Medical Association was founded for scientific purposes and to aid in solving the medical problems peculiar to the South. It has no direct affiliation with the various state medical organizations or the American Medical Association, although membership in a county and state medical society is a prerequisite. It has no legislative functions and has not been connected in any way with medical legislation in the states and national governments. The Southern Medical Association has made a record of splendid achievement and is the pride of the progressive physicians of the South.

I have selected for my title "Fifty Years of Progress" and in an effort to show you the really great progress that we have made in the past fifty years I went through our Journals, beginning at Number 1, Volume 1, right down to the current volume. It was a very interesting and educational excursion. There were many, many very interesting articles encountered in almost every number, a great many of which will be quoted. Some will be direct quotes, while others will be a condensation of longer articles.

My first and probably most important quote is an editorial from the Journal of July, 1908.

*Presidential Address, Presented at the First General Session, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

"Likewise our books, our files of journals that contain so much learning first-hand are wasted. The old physician or the sick physician forgets their value and leaves them to be sold as junk or waste paper, or to be burned by lay hands when a single clause in the will would settle them in the local medical society, the state society, or the nearest medical school, where numbers are hungering for their rich contents. We are wasting our treasures."

How true this is and how easy to correct. So gentlemen, please see that your will contains a clause which will place your journals and books in the proper place for continued education of those who follow us. Please see that they are not burned or sold for junk. As all accredited hospitals must maintain a medical library, maybe it would be advisable to leave our medical library to our favorite hospital. All one has to do to realize the great value of these old journals and books is to do as I have done, go through them. You will be surprised at the wealth of knowledge they contain.

The Birth and Early History

The Southern Medical Association was born October 2-3, 1906, in the Read House in Chattanooga, Tennessee. Dr. Giles C. Savage, President of the Tennessee State Medical Society, called the meeting requesting the Presidents of the Mississippi, Louisiana and Florida State Associations to send delegates to this meeting which was one day before the annual meeting of the Tri-State Society of Alabama, Tennessee and Georgia. After a conference the committee of delegates prepared the following resolution for the organization of a Southern Medical Association to be formed from the territory comprised in the states of Mississippi, Tennessee, Georgia, Alabama, Louisiana and Florida, which states by reason of their geographical location and similarity of population, naturally fall into a congenial relationship.

"We recognize that a greater opportunity for self-improvement and achievement in the realm of scientific research is required by the

progressive and cultured physicians of this district than is afforded by the States' Societies, and which, because of its large membership, is denied them in the American Medical Association. We believe that the profession as a whole will be benefited by such a society and assuredly that the members of this organization will have excellent opportunities to develop their talents. We believe that such an organization will be a long stride forward in perfecting the plan of organization which has been so splendidly carried out by the American Medical Association, and bring all the members in the district into closer touch and more perfect harmony with each other and the national association.

To accomplish this plan more perfectly and successfully, we therefore recommend that the Tri-State Medical Association of Tennessee, Alabama and Georgia hereby agree to merge itself into this larger body and hereby, become the nucleus for its formation. In so doing, its sphere of usefulness will be enlarged and its members will all be brought into direct affiliation with the American Medical Association.

We recommend that the name of this organization be the Southern Medical Association. We invite the careful consideration of the medical profession of the states above mentioned, to the reasons given therefor, and extend a cordial invitation to them to join with us in making this one of the most influential and important bodies of medical men in the United States."

Dr. H. H. Martin, Savannah, President of the Georgia State Society; Dr. Walter W. Crawford, Hattiesburg, President of the Mississippi State Society; and Dr. Jere L. Crook, Jackson, Tennessee, acting for Dr. Savage, were named as a committee to form a tentative constitution and by-laws for the new organization with the idea that it be considered a Southern District of the American Medical Association and present it to the Tri-State Medical Association of Alabama, Georgia, and Tennessee at its annual meeting in Chattanooga the following day. It was the hope and purpose of this committee that this small body of two hundred members founded by Dr. J. B. Cowan, Tullahoma, Tennessee, would agree to merge itself into a larger group of six states consisting of Louisiana, Mississippi and Florida in addition to the original Tri-States of Alabama, Georgia and Tennessee, the new association to be known as the Southern District Branch of the American Medical Association. These were the suggestions made to all three of the committee members by Dr. G. C. Savage, President of the Tennessee State Medical Association.

The committee unanimously decided to depart from instructions and to draft a tentative constitution for a Southern Medical Association, entirely independent of the American Medical Association which would eventually embrace all sixteen southern states and the District of Columbia. They worked the entire night on the preparation of the document in order to have it in shape to present to the Tri-State Meeting the next morning. That document was so clear and comprehensive that it was not amended for 20 years and there have been few changes in it to date. One of the best portions of the Constitution, Article 6, Section 3, has to do with the Council. The Councilors shall be appointed by the President, one from each state, shall serve for five years and shall not be eligible for reappointment. This assures a continuous infusion of new blood into that body which cannot wither and die with old men being continuously reappointed.

The chief obstacle to the plan was the opposition of Dr. J. B. Cowan, founder of the Tri-State, who naturally was loath to destroy his own brain child. But after a very ardent plea by Dr. Crook, Chairman of the Committee, which was ably and enthusiastically supported by Dr. Crawford and Dr. Martin, it was passed unanimously after which Dr. Cowan said, "Mr. President, after listening to the plea of these ambitious young doctors who have asked for a chance to try their wings over all of Dixieland, I move that we adopt this tentative constitution as a whole, without changing one jot or one title, and thus was born the Southern Medical Association."

There was only one condition imposed, which was that the respective State Medical Associations at their next annual meeting should approve. This was done in 1907 and thus the organization became a permanent one.

Dr. H. H. Martin of Savannah, Georgia, was elected President. Birmingham, Alabama, was selected for the next meeting to be held

on the first Tuesday in October, 1907. The next meeting was held in Atlanta and an article publicizing this meeting read as follows:

"The Birmingham meeting was not largely attended for the one single reason that the railroads gave us no rates; but from a scientific and social point of view the meeting was a grand success. There will be railroad rates for the Atlanta meeting, therefore, the attendance will be large. The programs will be full and rich, therefore the meeting will be a most profitable one."

In the very early days the railroads would grant reduced rates for a convention if there was in attendance a certain minimum number. You bought a one-way ticket to the convention city and were given a receipt or a certificate showing that a one-way ticket had been purchased. If you actually attended the convention and the required minimum number was in attendance, we so certified and then you could give the agent at the convention city the certificate and buy a return ticket for one-half the regular fare, which made it a one and one-half fare for the round-trip. This plan of reduced rates was in vogue for quite a long time in the earlier years.

When the Association was founded in 1906, there were three Sections, Medicine, Surgery and Ophthalmology and Otolaryngology. At that time the profession in the larger southern centers was divided mainly into Physicians, Surgeons, and Eye-Ear-Nose and Throat men. A man usually specialized in surgery only after he had built up a fairly large general practice. During these early days, the growth of specialism was as striking as the growth of the Association itself. Each time a new Section was established, there was opposition to it. Some doubt of its need existed until after the first meeting, after which there was never a question of dropping it. The date and place of origin of the Sections we now have are as follow:

Public Health, 1912, Jacksonville, Florida.

Industrial Medicine and Surgery, 1913, Lexington, Kentucky.

Pediatrics and Gastroenterology, 1917, Memphis, Tennessee.

Urology, 1919, Asheville, North Carolina.

Obstetrics, Orthopedic and Traumatic Surgery and Radiology, 1920, Louisville, Kentucky.

Neurology and Psychiatry, 1921, Hot Springs, Arkansas.

Dermatology and Syphilology, 1922, Chattanooga, Tennessee.

Pathology, 1923, Washington, D. C.

Gynecology, 1928, Asheville, North Carolina.

Allergy, 1933, Richmond, Virginia.

Proctology and Anesthesiology, 1937, New Orleans, Louisiana.

General Practice, 1941, St. Louis, Missouri (which by the way, was the first section on General Practice in any medical association).

Physical Medicine and Rehabilitation, 1942, Richmond, Virginia.

At the Hattiesburg meeting in 1911 it was decided to expand the Association to include the entire South. Mr. C. P. Loranz was elected Business Manager in 1912 and in 1921 upon the resignation of Dr. Seale Harris, he became the Secretary-Treasurer and General Manager and continued to fill these positions until November 30, 1954. He was succeeded by Mr. V. O. Foster as Executive Secretary-Treasurer and Mr. Robert F. Butts as Business Manager. Mr. Loranz was made Advisor and Professional Relations Counselor, which post he still holds and as usual, is doing a wonderful job. To talk about the Southern Medical Association and its progress over the years without paying tribute to the one individual who has been responsible for its growth and success would be heresy. No man ever served any organization with greater zeal and more devoted leadership than Mr. C. P. Loranz did for 42 years. He has forgotten clocks and watches in giving everything he had and more in carrying on his duties. All he thought about was the Southern Medical Association and what he could do to improve it and the cause of medicine in the South. He was responsible for every detail of our meetings. He arranged the meeting places, the program, the meeting rooms, the exhibits and all the other many details which make a successful meeting. The social side of the meeting which is the spirit of the Southern, is one of our greatest assets. C. P. arranged for the Alumni, Fraternity, Section and other group parties. He has even been responsible for arranging some of the private parties

which mean so much to all of us who regularly attend the Southern. It is here where we renew old friendships and create new ones. These friendships not only last, but become more firmly cemented through the years. I have on many occasions referred to C. P. as "Mr. Southern Medical" which he really is. At the Miami meeting in 1948, the Council and Board of Trustees presented to C. P., a Silver Service as a token of their appreciation for a job well done.

In 1911, when the Association expanded to include the entire South, the Association began publishing the Bulletin of the Southern Medical Association which is issued four times a year and is mailed to all members of state and county medical societies in the territory. This is published wholly to promote interest in and to expand the membership of the Southern Medical Association.

In 1906, the membership was a few hundred. In 1911, about 900. In 1921, about 6,500 and in 1955, about 10,000.

The principal difference in the early meetings and the more recent ones was mainly in the number of men in each Section capable of discussing the papers intelligently. Where formerly there was only a handful of such persons in each Section, the number has increased a hundred-fold.

Our growth in recent years has not been as rapid as formerly. This is due, entirely to the increasing number of medical meetings. There is not a specialty which does not have a national society and in addition, there are numerous Sectional, Regional and Interim meetings of our larger national societies. These associations are the direct result of specialism. Many of us find it advisable to belong to one or more of our special societies. This increase in special societies means increasing competition for the Southern. Therefore, to maintain our position among the world's leading medical societies it will be necessary for us to promote and maintain programs of sufficient scientific interest to attract doctors to our meetings. If we can attract a new member or an inactive member to one meeting, he will discover that the Southern has something which none of the other societies possess. This something will not only help us hold our own in the growing competition, but we will continue to grow bigger and better. Once a doctor has attended a Southern meeting he will never want to miss another.

At the Jacksonville meeting in 1912, the Board of Trustees was created by the Council and the first six immediate Past-Presidents were selected to man the Board. This policy has been continued since that time.

There was no meeting of the Southern Medical Association in 1918 because of the influenza epidemic.

In 1944, for the first time in the history of our Association, a President died during his term of office, Dr. William Turner Wooton of Hot Springs, Arkansas. He was succeeded by Dr. James A. Ryan of Covington, Kentucky.

In June of 1945, Dr. Edgar G. Ballenger of Atlanta, Georgia, died in office. He was succeeded by Dr. E. Vernon Mastin of St. Louis, Missouri.

In 1940, the President-Elect, Dr. Quitman V. Newell of St. Louis, Missouri, died in office.

Ladies and Gentlemen, I think we have been very fortunate over the past 50 years to have had only two presidents die during their term of office, especially when you consider that most of us are getting along in years when we achieve this honor.

At the annual meeting in New Orleans in 1924 a Woman's Auxiliary to the Southern Medical Association was organized. Mrs. Seale Harris called the meeting which has functioned splendidly since its beginning and has grown with the organization. The ladies have added much interest to the annual meeting with their special functions. I am sure it is the wish of everyone that the Woman's Auxiliary will continue to grow and keep up its good work.

The Southern Medical Journal

Dr. Raymond Wallace of Chattanooga was made Secretary-Treasurer of the Southern Medical Association at the organization meeting and served for one year. At the Birmingham meeting in 1907, Dr. Oscar B. Dowling of Shreveport, Louisiana, was named Secretary and the Shreveport Medical and Surgical Journal, of which he was Editor, was made the official organ. He held this position until his resignation in 1909 when Dr. Seale Harris, of Mobile, Alabama, was elected Secretary-

Treasurer and his Journal, The Gulf States Journal of Medicine and Surgery, became the official organ. In 1910, the Southern Medical Journal of Nashville, Tennessee, an independent Journal, first published in July, 1908, under the editorial guidance of Dr. John A. Witherspoon, was acquired by Dr. Harris and Associates and combined with the Gulf States Journal of Medicine and Surgery. This merger afforded an official organ of outstanding merit and has been published since that date as the Southern Medical Journal, Journal of the Southern Medical Association.

The Journal of July 1908, contained 100 pages of scientific material and published some of the papers of the Southern Surgical and Gynecological Association. The March 1909 number was named the Southern Surgical and Gynecological Number and contained only papers of those members. The January 1910 number was the same.

In February, 1911, Dr. Harris became Editor-in-Chief of the Journal in addition to his duties as Secretary-Treasurer. Dr. H. A. Moody of Mobile served as Managing-Editor until his death in 1916, when Dr. M. Y. Dabney was made Associate Editor and later became Editor-in-Chief on the resignation of Dr. Harris in 1921. In 1929, Mrs. Eugenia B. Dabney was made Associate Editor. The Dabneys served until November 30, 1954, when they asked for retirement and Dr. R. H. Kampmeier of Nashville, Tennessee became Editor.

The following editorial appeared in 1911, and I think it well worth quoting:

"The Southern Medical Journal was born at an opportune time and we feel confident will find a ready welcome in the medical literature of the South, which has long needed a medium of this kind that the best thoughts of her medical men shall not only be given to the world, but it is essentially the object of this Journal to build up and foster medical thought as clothed by environment and such changes as would naturally come from local conditions and climatic influences. It has long been known that even the most common diseases are more or less changed, or present different features in the South, and indeed, in certain localities of the South far different from that in higher parts of our country. It is because of these facts, after numerous requests on the part of the profession in the South, that the staff of this Journal has organized itself, regardless of school influences or personal interests in the sincere determination to keep its pages open to the best from whatever ethical source it may come, and to give to the profession of the South, not only this medium for the registering of their own thought, but to stand firm in the great principles of ethical journalism. We beg to assure the profession of the South that no articles of an advertising nature and certainly no advertisements of a proprietary nature, shall never pollute the pages of this Journal. We have determined, even if it causes a financial sacrifice, that the pharmaceutical houses of this country shall never gain control of this Journal, and can only use its medium of advertising for strictly ethical purposes. We hope also that the profession of the South will avail themselves of this medium, and give to the world the many excellent thoughts and the many brilliant successes which have characterized the medical men of this section of the country since the time of Ephriam McDowell, Marion Sims Long, of Georgia and many others to whom we can point with pride as pioneers in the profession and to whom the entire medical world is under lasting obligations. If the young men of the South would take these examples as their criterion, and do more original work or even give to the world the original work they are now doing, it would reflect great credit upon their own section of the country and place the profession of the South on the proper footing with their medical brothers of the North and if this Journal can be the means of inciting greater labor, more earnestness and more thorough work on the part of its clientele, it will have accomplished the purpose for which it was created.

While its pages are open, as has been said, to all legitimate articles; yet its staff, being mindful of its duty to its readers, will claim the right to return all manuscripts that for any reason they may not feel justified in publishing. So that with these few introductory remarks, we enter the field of journalism with clean hands and ethical principles and by these we hope to receive the endorsement and patronage of the medical men who desire to keep abreast with the times."

At the Hattiesburg meeting in 1911, Dr.

Harris reported the Journal free of debt for the first time and also agreed to allow the Southern Medical Association to acquire the Journal at the end of 10 years. The Association was to pay Dr. Harris and other stockholders ten times the average net earnings for the last three years of that 10-year period, in ten annual payments without interest. In 1921, the Association exercised its option and acquired the Journal, the stockholders being paid in 7 years instead of the stipulated 10 years.

In November 1912, an editorial suggesting the length of papers to be read before the Sections and published in the Journal to be twenty minutes and four or five pages.

On July 1, 1915, the Journal moved from Mobile to the Empire Building in Birmingham. On December 1, 1915, the President's photograph appeared in the Journal for the first time. It has been an annual feature since then.

It was in this issue (December, 1915) that the United States Public Health Service announced the discovery of the cause of pellagra as a deficiency in diet. The experiments were carried out at the Mississippi State Penitentiary under the direction of Drs. Joseph Goldberger and G. A. Wheeler. Twelve convicts were asked to volunteer for the experiment with promise of full pardon. Of the eleven who volunteered, six developed pellagra.

The first article on pellagra in the Southern Medical Journal appeared in 1908 when Dr. J. M. King of Nashville reported some cases. Previous to this time, only sporadic cases had been reported in the United States. The etiology was supposedly protozoa or corn. For the next thirty years innumerable articles on pellagra appeared in the Journal. An editorial in the March 1938 number quotes the finding of a cure for pellagra from a paper by Spies, Cooper and Blankenhorn, read before the Central Society for Clinical Research in Chicago in November, 1937.

In the early numbers, malaria was very prevalent and many numbers contained only articles concerning malaria. This continued for many years and then the number of papers on malaria began to lessen until at the present time we see only an occasional one.

In the Journal for October, 1932, there was an article by Dr. Wm. J. Mayo entitled, "Southern Surgeons, Recollection of My Association with Them." This paper was read before the Southern Surgical Association in December, 1931, at their meeting in White Sulphur Springs, West Virginia. It cites J. Marion Sims of Montgomery, Alabama, David Yandel and Lewis S. McMurtry of Louisville, Kentucky, W. D. Haggard, Sr., and George Benjamin Johnston, of Nashville, Tennessee, Hunter McGuire of Richmond, Virginia, John A. Wyeth, who married a daughter of J. Marion Sims and who founded the first postgraduate school in America and also W. E. B. Davis of Birmingham, Alabama. He spoke very highly of all these gentlemen, paying high tribute to their ability in their special field of surgery. He told this story about William L. Rodman who was Professor of Surgery in Louisville, when he was called to Philadelphia to take the Chair of Surgery at Medico-Chi, now the postgraduate school of the University of Pennsylvania. Dr. Rodman was selected to represent the medical profession before the Pennsylvania State Legislature where a pernicious osteopathic bill was being heard. The attorney for the osteopaths said and repeated it many, many times throughout the argument, "The medical profession has built a fence around itself which is horse-high, bull-strong and pig-tight." Dr. Rodman, when he arose to answer, ignoring everything the attorney had said except that remark, replied, "Yes, it is perfectly true that the medical profession has built a fence around itself which is horse-high, bull-strong and pig-tight, but it is with no idea of excluding those who can enter through its scientific gates, but simply to keep out the jackasses." The bill was killed.

In the Journal of the Southern Medical Association of November, 1937, there appeared an editorial entitled "25 Years of Service." It told of C. P. Loranz' first 25 years of service and traced the beginning of the Southern Medical Association and told of the growth in those 25 years. It makes the title of "Mr. Southern Medical" even more appropriate for C. P. In 1912, when C. P. first started, there were only four Sections and less than 300 in attendance. At the Baltimore meeting in 1936, there were eighteen Sections and over 3,000 in attendance. Scientific exhibits increased from none to more

than 100 and technical exhibits from one-half dozen to over 100. "In his quarter century of work he has shown great tact, acumen, honesty of the purest variety and a genius for bringing together a group of physicians in whom he has inspired admiration, affection and respect." In synthesizing the innumerable side chairs of the large organic molecule of a useful scientific organization, few could have succeeded as he has. May its next 25 years be as fortunate.

In November, 1942, Mr. Loranz published a statement "30 Years of Service." In November 1952, he brought us up to date by adding "40 Years of Service." I hope I am around to read his statement, "50 Years of Service."

In 1937, 1938 and 1939, the Journal was publishing numerous articles about the first of the chemotherapeutic drugs, sulfanilamide. In 1938, an editorial about sulfanilamide appeared. In the 1940's articles concerning the antibiotic drugs began to appear. In July 1940, there was an editorial on Gramacidin, one of the first antibiotics obtained from soil.

In 1940-1941 articles and editorials of the other sulfa products began to appear: sulfadiazine, sulfapyridine, and sulfathiazole. These articles outlined their uses, benefits and dangers.

The first article about penicillin was an editorial in the Journal for May 1943. In July 1943, another editorial on penicillin. In July, 1944, an editorial on the treatment of syphilis by penicillin. From 1946, until the present, articles about penicillin became increasingly frequent. In 1947, there began to appear articles about the unfavorable reactions and complications of penicillin administration. These are continuing as you know.

In 1947, the antihistamines were introduced and many articles concerning their use and abuse has been appearing in the pages of our Journal.

Pellagra and malaria have almost disappeared from the journals as has typhoid, smallpox and diphtheria. It seems to be a continuing process as older diseases are conquered, new ones appear to take their place in the news. Allergy was rarely reported in the early journals, but now has a very prominent place. To the inhalants and ingestants have been added injectable materials as best illustrated by the newer antibiotics, for instance, penicillin, etc.

In the 1940's articles concerning the other antibiotic drugs began to appear. In almost every number there is a new one announced.

In recent years more articles on pulmonary and cardiac surgery are appearing. The Journal is always abreast of the times and in some instances, a little bit ahead.

Also articles on geriatrics are assuming a more prominent place. I suppose as more people in our increasing population reach 60 years or more, geriatrics may almost monopolize the pages of the Journal. While we do not have a Section on Geriatrics as yet, it undoubtedly will materialize. Last year in Houston, we had a wonderful Symposium on Geriatrics. It was so successful that we are having another one this year.

I have thoroughly enjoyed this year as your President. I hope that I have not bored you with my historical account of the Southern Medical Association and our Journal. While it was a lot of work, it also was a lot of fun.

In this city of Washington, D. C., in front of the National Archives Building, there is an inscription which seems to me to be a fitting conclusion to my report of our fifty years of progress: "What is past is prologue."

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BOOKS RECEIVED

Williams Obstetrics. By Nicholson J. Eastman, Professor of Obstetrics, Johns Hopkins University. Eleventh Edition, 1161 pages. New York: Appleton-Century-Crofts, Inc., 1956.

The Initial Management of Thoracic and Thoraco-Abdominal Trauma. By Lawrence M. Shefts, M.D., Associate Professor of Surgery (Thoracic), University of Texas Medical School, San Antonio; Assistant Professor of Surgery (Thoracic), Baylor University Medical School. 114 pages, American Lecture Series. Springfield, Illinois: Charles C. Thomas, Publisher, 1956.

Other People's Children. By Anna Judge Veters Levy, Judge, First City Court, New Orleans. 287 pages. New York: The Ronald Press Company, 1956. Price $3.75.

Textbook of Gynecology. By Emil Novak, M.D., Assistant Professor Emeritus of Gynecology, The Johns Hopkins Medical School; and Edmund R. Novak, M.D., Instructor in Gynecology, Johns Hopkins Medical School. Fifth Edition, 822 pages. Baltimore: The Williams and Wilkins Company, 1956.

Wire Brush Surgery. By James W. Burks, Jr., M. D., Associate Professor of Clinical Medicine (Dermatology), Tulane University School of Medicine. American Lecture Series, 154 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $6.75.

The Management of Fractures, Dislocations, and Sprains. By John Albert Key, M.D., Clinical Professor Emeritus of Orthopedic Surgery, University of Alabama School of Medicine. and H. Earle Conwell, M.D., Associate Professor of Orthopedic Surgery, University of Alabama School of Medicine. Sixth Edition, 1144 pages. St. Louis: The C. V. Mosby Company, 1956. Price $20.00.

Pharmacology and Oral Therapeutics. By Edward C. Dobbs, D.D.S., Professor of Pharmacology and Therapeutics, Dental School, University of Maryland. Eleventh Edition, 555 pages. St. Louis: The C. V. Mosby Company, 1956. Price $9.00.

Etiologic Factors in Renal Lithiasis. Compiled and edited by Arthur J. Butt, M.D., 385 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $12.50.

Procedure in Taxonomy. By Edward T. Schenk and John H. McMasters. Third Edition. 91 pages. Stanford, California: Stanford University Press, 1956. Price $3.50.

The Nature of Brucellosis. By Wesley W. Spink, M. D., 455 pages. Minneapolis: University of Minnesota Press, 1956. Price $8.00.

Dictionary of Poisons. By Ibert and Eleanor Mellan. 150 pages. New York: Philosophical Library, 1956. Price $4.75.

Nerve Impulse. Transactions of the Fifth Conference, September, 1954. Edited by David Nachmansohn, M.D., Professor of Biochemistry, Columbia University College of Physicians and Surgeons; and H. Houston Merritt, M.D., Professor of Neurology, Columbia University College of Physicians and Surgeons. 218 pages. New York: Josiah Macy, Jr. Foundation, 1956. Price $4.50.

Group Processes. Transactions of the Second Conference, October, 1955. Edited by Bertram Schaffner, M.D., University Seminar on Communications, Columbia University. 242 pages. New York: Josiah Macy, Jr. Foundation, 1956. Price $3.50.

The Support of Medical Research. A Symposium organized by the Council for International Organizations of Medical Sciences. Edited by Sir Harold Himsworth and J. F. Delafresnaye. 168 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $4.00.

Care of the Long-Term Patient. Vol. II of Chronic Illness in the United States, under auspices of Commission on Chronic Illness. 587 pages. Cambridge, Massachusetts: Harvard University Press for the Commonwealth Fund, 1956. Price $8.50.

Pediatrics. Edited by Donald Paterson, M.D., and John Ferguson McCreary, M.D., Professor and Head, Department of Pediatrics, The University of British Columbia. With 36 contributing authors. 620 pages. Philadelphia: J. B. Lippincott Co., 1956. Price $14.00.

Pelvimetry. By Herbert Thoms, M.D., Emeritus Professor of Obstetrics and Gynecology, Yale University School of Medicine. 115 pages. New York: Paul B. Hoeber, Inc., 1956. Price $5.00.

Urology and Industry. By Leonard Paul Wershub, M.D., Associate Professor of Urology, New York Medical College. 141 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $5.00.

Neurological Nursing. A Practical Guide. By John Marshall, M.D., M.R.C.P., M.R.C.P. ed., D.P.M., Senior Lecturer in Neurology, University of Edinburgh. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $3.75.

Progress in Radiobiology. Proceedings of the Fourth International Conference on Radiobiology Held in Cambridge on August 14 to 17, 1955. Edited by Joseph S. Mitchell, Barbara E. Holmes and Cyril L. Smith, Department of Radiotherapeutics, University of Cambridge. 550 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $12.75.

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SOUTHERN MEDICAL NEWS

ALABAMA

Dr. Tom D. Spies, Birmingham, Alabama, and Chicago, Illinois, was unanimously elected President-Elect of the Interstate Postgraduate Medical Association of North America by its Board of Trustees at the annual meeting of the Association in Cleveland, Ohio, in October. The Association is primarily a postgraduate teaching organization. Dr. Spies has spoken before it a number of times. Dr. Spies is Scientific Director of the Nutrition Clinic, Hillman Hospital, Birmingham, and Professor and Head of the Department of Nutrition and Metabolism, Northwestern University Medical School, Chicago.

Dr. Charles H. Paine, Decatur, has joined the Chemstrand Corporation as full-time plant physician.

DISTRICT OF COLUMBIA

Dr. Harry Davis Bruner has been appointed Chief of the Medical Branch of the Commission's Division of Biology and Medicine.

Dr. John D. Porterfield has been named assistant to the Surgeon General of the Public Health Service. He assumed his new duties on October 16.

Dr. Charles D. Shields took office as associate dean of the Georgetown University School of Medicine October 1.

The District Public Health Advisory Council has appointed Dr. W. Montague Cobb as chairman and Dr. Montgomery Blair, Jr., vice-chairman.

The George Washington University has appointed Rear Admiral Lamont Pugh as a university physician who will participate in the student health programs of the Health Administration under Dr. Richard B. Castell, Director.

The American Medical Educational Foundation has elected Dr. James E. Fitzgerald to Advisory Membership.

FLORIDA

Dr. David S. Howell, Miami, has been appointed to the Committee on Affiliation with the Food and Drug Administration for the American Rheumatism Association.

At a recent meeting of the American Society of Anesthesiology Dr. Ralph S. Sappenfield, Miami, was elected president-elect.

The Dade County Chapter of the American Academy of General Practice recently elected the following new officers: Drs. Leonard L. Weil, president-elect; Robert C. Piper, vice-president; Jack E. Keefe III, secretary-treasurer; and Vincent P. Corso, Board of Directors.

Drs. Carl E. Dunaway and Thomas W. Hutson were awarded certificates of Life Membership in the Dade County Medical Association at a recent meeting.

Dr. Thomas C. Butt, Orlando, has been appointed chairman of the Doctors' Division of the United Appeal of Orange County. He is also president of the Orange County Medical Society.

The American Association of Blood Banks has elected Dr. James N. Patterson, Tampa, as district director.

Dr. Leo M. Wachtel, Jr., Jacksonville, has been elected to the Board of Trustees of Bolles School in Jacksonville.

The Duval District Heart Association has elected Dr. Turner Z. Cason, Jacksonville, president.

Dr. Percy H. Guinand, Clearwater, has been elected president of the Pinellas County Medical Society. He succeeds Dr. Daniel F. H. Murphey.

GEORGIA

Dr. Fred H. Simonton is the new chairman of the State Board of Health. Other new members are Drs. Alex Little, Jr., Valdosta; A. M. Phillips, Macon; and Maurice F. Arnold, Hawkinsville.

New officers of the Georgia Heart Association are Drs. Ernest F. Wahl, Thomasville, president; J. Gordon Barow, Atlanta, vice-president; Goodloe Y. Erwin, Athens, president-elect; and A. Calhoun Witham, Augusta, secretary.

Dr. Joseph Boniface, Savannah, has been appointed instructor in the department of anesthesiology at the Medical College of Georgia.

Dr. W. D. Lundquist, Savannah, was elected president of the Georgia Tuberculosis Association at the meeting of the association held in Rome in September.

Dr. Robert H. Vaughan, Columbus, has been elected secretary-treasurer of the Georgia Trudeau Society. Dr. John H. Gross, Rome, is the new president-elect.

Dr. John F. Bertles, Atlanta, has been appointed a research fellow in medicine at Harvard Medical School.

Dr. Harry L. Cheves, Sr., Union Point, has been made a qualified fellow of the International College of Surgeons.

KENTUCKY

Dr. E. Franklin Hall, Ashland, is the new medical director for Greenup and Boyd counties.

Dr. J. C. McGuire, Greenville, has become associated with the Division of Local Health Services of the State Department of Health.

Dr. Edward B. Mersch, Covington, was elected president-elect of the Kentucky State Medical Association at a recent meeting of the Association. Elected vice-presidents were: Drs. Karl Winter, Louisville; Carl Norfleet, Somerset; and Charles Yancy, Hopkinsville. Dr. Woodford B. Troutman, Louisville, was elected secretary.

Drs. Hugh Mahaffey, Richmond, and L. O. Toomey, Bowling Green, were elected chairman and vice-chairman respectively of the Council of the Kentucky State Medical Association at the recent annual meeting.

Dr. Joseph T. Molony, Covington, received the 1956 honor award for distinguished service in the field of obstetrics.

Dr. J. T. Coleman, Frankfort, has been honored as Kentucky's outstanding general practitioner of the year.

Dr. Russell Teague has been appointed chairman of a newly appointed Commission on Indigent Care.

Dr. Clyde C. Sparks, Ashland, has been elected to serve a three-year term as Speaker of the House of Delegates for the Kentucky State Medical Association. Dr. George Pedigo, Louisville, succeeds Dr. E. W. Jackson as Vice-Speaker.

Dr. Guy Aud, Louisville, was elected editor of *The Journal of the Kentucky State Medical Association* by the Council at its recent meeting.

Dr. John Ball, Louisville, succeeds Dr. Joseph Goldstein as president of the Kentucky Psychiatric Association. Other officers of the Association are: Drs. James Lowry, Lexington, vice-president; Logan Gragg, Lexington, secretary-treasurer; and E. E. Landis, Louisville, delegate to the American Psychiatric Association.

At a recent meeting of the American College of Surgeons the following Kentucky surgeons were honored: Dr. Daniel C. Elkin, Lancaster, was installed as president and Dr. Arnold Griswold, Louisville, as vice-president.

Drs. Clyde C. Sparks, Ashland, and Branham B. Baughman, Frankfort, have been named directors to the Kentucky Medical Foundation.

LOUISIANA

Dr. Louis Ochs, Jr., has been elected vice-president of the American College of Gastroenterology.

The following became fellows in the American College of Surgeons at the College's annual clinical congress: Drs. Arthur C. Davidson, Edward T. Haslam, Homer D. Kirgis, Fred W. Maher, Robert P. Morrow, Jr., Frank G. Nix, Melvin M. Rosenthal, Malcolm P. Schwarzenbach, Joseph A. Vella and Charles R. Walters.

Dr. Bernard Weinstein has been named a member of the executive committee of World Fertility Council, which is the executive council of the International Fertility Association.

Drs. Ralph H. Riggs, Shreveport, and H. Ashton Thomas, New Orleans, have been presented the Golden Head Mirror Honor Award of the American Rhinologic Society. They received this award "for

Continued on page 64

BOOK REVIEWS

Pathology Seminars

Edited by Robert S. Haukohl, M.D., Assistant Professor of Pathology, Marquette University School of Medicine, Milwaukee, Wisconsin, and W. A. D. Anderson, M.D., Professor of Pathology and Chairman of the Department of Pathology, University of Miami School of Medicine. 191 pages. St. Louis: The C. V. Mosby Company, 1955. Price: $10.00.

In 191 pages, Professors Haukohl and Anderson have presented an interesting variety of material for consideration. The illustrations are excellent, the summaries and comments are brief and to the point, and the clinical and pathological implications are ably presented.

The only deficiency, and this may be intended, lies in the specialization of the material covered. The sections on pathology of the skin and tumors of the nose and throat are especially recommended.

Old Age in the Modern World

Report of the Third Congress of the International Association of Gerontology, London, 1954. 647 pages. Baltimore: Williams and Wilkins Company, 1955.

This book is a report of the Third Congress of the International Association of Gerontology, held in London in 1954. There are a great number of individual reports by authors from various "western" nations of the world dealing with most of the major problems of ageing which concern both the individual and the community.

There is much to be learned from the various authors which could find application in the United States, although the problems of ageing do vary from nation to nation and treatment has to be individualized according to the needs of each community.

A listing of the chapter headings alone indicates its comprehensive scope. They are: Age and Society, National Programmes, Integration of Plans for the Care of the Aged in Health and Infirmity in the United Kingdom, Nutritional Aspects of Ageing, Tissue Changes, Cancer, Endocrinology, Experimental Studies of Changes in Performance with Age, Employment of Older Workers, Surveys, Neuropsychiatry, Cardiovascular Diseases, Clinical Problems, Residential Care, Community Activities, Education for Later Maturity in the U. S. A. and General Aspects of Ageing. The book is not mean to be a text but, the wide coverage of many of the aspects of ageing should make it an excellent reference for those with special interest in this subject.

Your Health Today

Harper's Series in School and Public Health Education, Physical Education, and Recreation. By W. W. Bauer, B.S., M.D., Director of The Bureau of Health Education of the American Medical Association. Edited by Delbert Oberteuffer. 514 pages, illustrated. New York: Harper & Brothers, 1955. Price: $5.00.

This book is an excellent presentation of modern ideas concerning health and health education. The author delivers his message in a simple, unbiased way. The absence of bias is best illustrated by the sections on tobacco and alcohol. Each of the major health problems is treated briefly but fully enough for the student to obtain a good idea of what the non-professional person needs to know from personal and community aspects.

The preventable diseases are discussed and for those diseases which are not preventable in this day and age, a plea is made for early detection and a common sense approach on the part of the individual. Accidents and ageing, two problems becoming more and more important in our society, are dealt with adequately.

This book should prove very worthwhile as a text for students at the college level and as a source of general information for families and the public in general.

The Thyroid

Edited by Sidney C. Werner, M.D. 771 pages. New York: Paul B. Hoeber, Inc., 1955. Price: $20.00.

This volume though titled "The Thyroid" could perhaps be even more accurately given the title "Medicine With Emphasis on the Thyroid," for it is so all inclusive. Its sixty contributors represent a great portion of the apex in American research and clinical medicine. This volume contains authoritative views covering all aspects of thyroid anatomy, physiology, pathology, and therapy. The interrelationships of the thyroid in health and disease with all other body systems are completely presented.

The values, flaws and pitfalls of the various new laboratory aids are carefully explained, along with the potential sources of laboratory error. The various forms of new therapy for thyroid dysfunction are discussed completely. The index of this volume is satisfactory and its bibliography is more than adequate.

This text would serve as an invaluable addition to one's endocrine library on endocrinology. A more complete survey of the thyroid and its relation to the entire body systems cannot be imagined by this reviewer.

The Practice of Dynamic Psychiatry

By Jules H. Masserman, M.D., Professor of Neurology and Psychiatry, Northwestern University. 790 pages. Philadelphia: W. B. Saunders Company, 1955. Price: $12.00.

This is not a textbook of psychiatry in the usual sense, but a rather detailed elaboration of the practical applications of Dr. Masserman's "biodynamic" teachings to the clinical practice of psychiatry. A relatively small portion of the volume is devoted to the description of various diagnostic categories. The emphasis is placed on the total evaluation of the patient in understanding the interaction of personality, mechanisms of defense, and environmental influences in the symptoms manifested by the patient.

The book is divided into five sections. The first of these contains an excellent description and discussion of the purpose and technics of psychiatric history taking. Many practical points in securing an adequate history and mental status evaluation are to be found in this section. Included also is a discussion of the basic principles and rationale of psychologic testing for diagnostic purposes and personality assessment. In the second section, evaluation of clinical syndromes is presented. The emphasis is placed on an understanding of the dynamic functions involved, rather than in symptom description. Part three deals with practical consideration of records, consultations, reports to referring physicians, and personnel evaluations. Forensic aspects of psychiatry met with in practice are discussed and illustrated. The fourth section is a brief discussion of the dynamics of emotions in light of the author's theories which he has previously organized into the system he calls "Biodynamics." The final section makes up approximately one half of the volume and is devoted to the practice of a dynamic psychotherapy. Historical development of psychotherapy and the various schools of psychoanalysis are discussed. Therapy as seen in light of the author's theories of biodynamics is discussed with liberal use of case history material. Many practical points of therapy technics are illustrated.

This book will be of much value to psychiatric residents, psychiatrists, and to physicians in general who have a basic knowledge of psychiatry. The material presented is naturally influenced strongly by the author's concepts and a background of basic psychiatric knowledge is needed to evaluate and utilize the wealth of useful information relating to all phases of the practice of psychiatry and psychotherapy that is presented in this volume.

Biochemical Mechanisms in Inflammation

By Valy Menkin, M.D., Head of Department of Experimental Pathology, Agnes Barr Chase Foundation for Cancer Research, Associate Professor of Experimental Pathology, Temple University School of Medicine. American Lecture Series, 412 pages, illustrated. Second Edition. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price: $9.50.

The book presents an extension of the concepts elaborated in the author's original "Newer Concepts in Inflammation." The attempt is made to explain the very complex biologic phenomena of the inflammatory reaction by analysis of the actions of substances liberated by injured cells. The role and actions of leukotoxine and other compounds isolated by the author from the inflammatory exudate are set forth,—largely in the light of experimental work of the author and others. The general as well as the local reactions of the organism to injury are explained on the basis of biochemical components, definable by such means as paper chromatography. The release of one or possibly several growth promoting factors from injured cells is presented as the stimulus for repair. The anti-inflammatory action of adrenal cortical hormones is considered at some length and explained in relation to another factor concerned with increased capillary permeability in the later stages of the inflammatory reaction—this substance being referred to as exudin.

Over all this attempt to explain all aspects of the inflammatory reaction on the basis of the presence of numerous and sometimes not too well defined sub-

stances in the exudate is well done. Certainly this approach is logical and may represent the ultimate as far as elucidation of this basic process is concerned. Some difficulty is encountered at the present time however in regarding inflammation as no more or no less than a series of well-defined biochemical reactions. The reference list is good and this work should be available to anyone concerned with the teaching or investigation of the inflammatory reaction.

Diseases of the Ear, Nose and Throat

By William Wallace Morrison, M.D., Professor of Otolaryngology and Director of Department, New York Polyclinic Postgraduate Medical School and Hospital. Second Edition. 756 pages, illustrated. New York: Appleton-Century-Crofts, Inc., 1955.

This is a small textbook of Otolaryngology as textbooks go, but the author has taken great care to make it a very helpful and practical guide for the medical student and for the general practitioner. A minimum of theory is included, but each chapter is filled with information which is useful to the physician who encounters otolaryngologic problems in his everyday practice. Common conditions are stressed rather than rare diseases. Treatment is briefly outlined and only one or two preferred methods of treatment are given for each of the diseases discussed. These treatments are generally ones that are specific or have stood the test of time. There is no waste of space in long and involved descriptions of difficult surgical procedures which should be attempted only by a surgeon trained in this type of work. Such procedures are described quite briefly and simply. Simpler operations which can and should be employed by the general practitioner are fully described and illustrated. All of the illustrations were drawn by the author. Although he is not a skilled medical artist the illustrations are well drawn and easily understood. Dr. Morrison's book can be highly recommended for undergraduate medical students and general practitioners who are interested in problems of the ears, nose and throat and who wish to treat many of these problems.

Transplantation of Tissues

By Lyndon A. Peer, M.D., Clinical and Research Director, Rehabilitation Center for Plastic and Reconstructive Surgery, St. Barnabas Hospital, Newark, N. J. Vol. 1. 421 pages. Baltimore: The Williams and Wilkins Company. Price: $13.50.

In the introductory chapter of his book "Transplantation of Tissues," Dr. Peer makes the following statement which I feel is very significant. "It is not uncommon to observe a skilled surgeon who performs an excellent operation from a technical standpoint but who transgresses one of the biological laws of tissue transplantation with an operative failure as the result." To a surgeon in our field, the application of these laws, almost daily, is a necessity for success, and all surgeons will certainly profit by a thorough knowledge of them.

In my work it has been my policy not to transplant tissue unless I am certain that it will remain permanently viable. Dr. Peer has supplied us with the first treatise which gives the reasons for avoiding the errors in judgment commonly committed in the choice of materials for reconstruction, either homo- or autografts, fresh or preserved. Chapter by chapter, with a very full bibliography appended to each, he has presented the whole picture of the fate of the various materials at hand for grafting, culling the pertinent facts concerning each from a voluminous literature. Cell viability and culture in general, cartilage, bone, fascia, soft tissues, etc., are fully treated. He has accomplished this in his own inimitable, fair and original way, directly to the point, with diagrammatic sketches to impress on the reader the fate of tissue in animal experiments and in humans.

Long a good friend of mine, Dr. Peer, or "Lyn" as we familiarly know him, has chosen a subject which I believe to be of signal importance just now, when so much recent attention is being directed to skin, fetal membrane, arterial, bone, and even gland transplantation. It is my belief that a careful study of a book which is so comprehensive and thorough, not only will stimulate further efforts in many promising directions, but will also prevent the unwise use of research funds. In an impartial but authoritative manner, he shows the futility of pursuing work in certain other directions, for example on certain heterotransplants to which an undue amount of time has probably been devoted in the past.

Through the study of a vast amount of literature and extensive personal observation, through years of operative work in his own fine clinic and first hand observation of the results of others, the author has given us the benefit of his broad knowledge and tremendous experience in a field in which so much has been equivocal and obscure. He has a delightful manner of writing on such technical considerations as the nature of various forms of cells and the behavior of different varieties of grafts. The great reliability of his conclusions is based upon his essential fairness and intellectual honesty, compiled with his wide research and surgical experience.

I have found the volume fascinating reading. It is beautifully illustrated and there is just enough repetition to make the facts easy to remember. Having worked at one time with Dr. René Leriche, I was particularly impressed, among his other fine discussions, with Dr. Peer's splendid treatment of the "Tissue Replacement Theory versus The Cell Survival Theory" and with his fine presentation of the clinical uses of grafts of various tissues. Though his opinions are authoritative, he expresses them with a humility and deference to the views of others which shows his true greatness. To me nothing in the volume shows this more strikingly than his words in the opening chapter, describing how even a medical man with only a compound microscope, who practices in an outlying area away from a medical center, can "still contribute valuable knowledge about the behavior of human tissue cells in transplanted grafts," employing only his own individual powers of observation. Here is expressed the spirit of the real investigator and student of natural laws. In this spirit, he has given us his book on tissue transplantation which I regard as a classic in this field.

Dr. Peer's book is a *sine qua non* for plastic surgeons. Students and research workers alike will find

the volume an invaluable reference work. It will prove itself an important aid to those in the vascular field who perform arterial grafts, to general surgeons and orthopedists who do fascial and bone grafting as well as to those medical men who are forward thinking enough to be interested in such subjects as gland transplantation.

Clinical Roentgenology, Volume III.
The Lungs and the Cardiovascular System
Emphasizing Differential Considerations

By Alfred A. deLorimier, M.D., Radiologist, St. Francis Memorial Hospital and Consultant in Radiation Therapy for the U. S. Public Health Service at the U. S. Marine Hospital, San Francisco; Henry G. Moehring, M. D., Radiologist, Duluth Clinic; and John R. Hannan, M.D., Radiologist, Lake County Memorial Hospital, Painesville, Ohio. 492 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price: $20.50.

The book is a well-organized work on the clinical radiographic diagnosis of congenital and developmental changes and pathologic changes secondary to disease. The thorax is divided into its anatomic components such as thoracic cage, diaphragm, mediastinum, pleura, lung and heart. Each is considered individually with the normal anatomy and general information followed by anatomical variations and the changes produced by various diseases found clinically to involve that part.

The lung is discussed under conditions affecting its anatomic subdivisions, i.e., vascular, lymphatics, bronchi and parenchyma. The heart is considered under congenital malformations of the heart and great vessels and acquired heart disease. The pericardium and aorta are dealt with separately.

Each entity is presented under General Considerations, Roentgen Manifestations, Clinical Corroboration, Laboratory Corroboration and Differential Considerations. The material under each heading is pertinent and concise, stressing the common, outstanding clinical characteristics of the disease with its roentgen manifestations and the differential factors. Thus a comprehensive coverage is achieved and an excellent guide and aid to diagnosis for the roentgenologist is presented.

The illustrations are good in quantity and quality. References are well selected and conveniently placed.

Disorders of Character. Persistent Enuresis,
Juvenile Delinquency and Psychopathic Personality

By Joseph J. Michaels, M.D., Boston, Massachusetts. 148 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price: $4.75.

Dr. Michaels begins his book with his observations in juvenile delinquents of the high incidence of persistent enuresis and sets about to investigate this relationship more specifically.

As an approach to the problem he presents statistical data emphasizing that enuresis is a reflection of an ill-balanced personality rather than an isolated finding. In support of this he finds a positive correlation between persistent enuresis and other neurotic traits, antisocial traits, abnormal EEG patterns. The incidence of positive family histories for enuresis points out the genetic aspects.

Further analysis of the data leads to the conclusion that enuresis may be an expression of a general deficiency of inhibition seen on several levels of personality integration. The premise is presented that, on a physiological level, enuresis represents a psychosomatic predisposition giving rise to a pattern of "lack of control" which permeates the entire personality and is seen neurophysiologically as a "short-circuiting" leading to the well-known acting out of the character disorder. It is held that on other levels the persistent enuresis represents a maladjustment in the "biopsychic" sphere whereas the related delinquent behavior, in the "psycho-social" sphere.

From the material the possibility of delineating an *impulsive* type of juvenile delinquent (with persistent enuresis) as compared to *compulsive* or neurotic type in which, in the former, there is much more primitive immature adjustment, is presented. The way is thus opened for broadening our concepts of libidinal development, psychoanalytically, to add the impulsive character to Freud's erotic, compulsive, and narcissistic types. He points out that for full investigation of this concept, the urethral zone should be more fully assessed psychoanalytically. The relationship of these impulsive character disorders to traumatic neurosis and epilepsy is demonstrated.

The author presents the hypothesis and supporting evidence in a clear and concise manner, raises unanswered questions opened by his formulations and points out those areas in which further investigation is needed. An excellent bibliography is among the book's assets. The work is recommended for study by all students of the science of human behavior.

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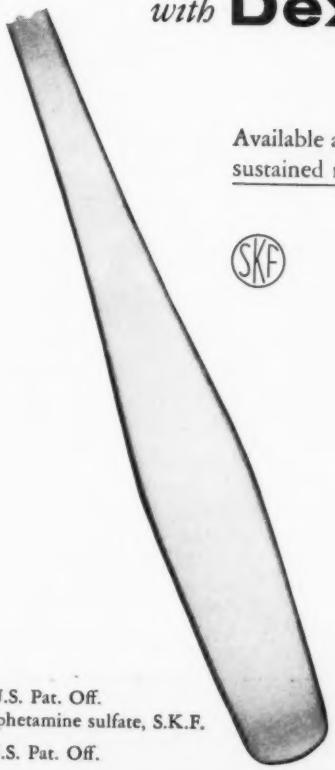

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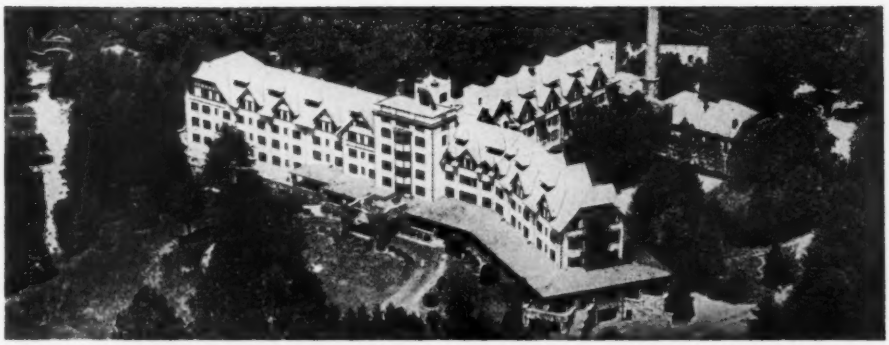

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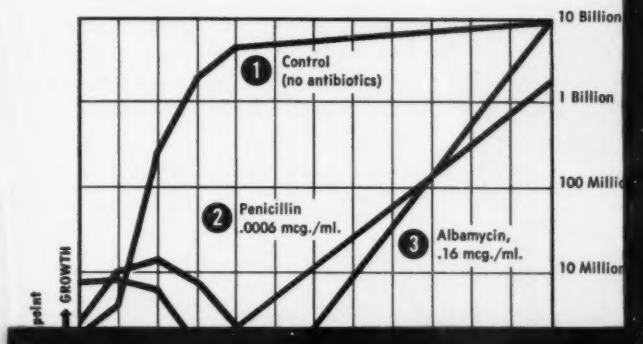

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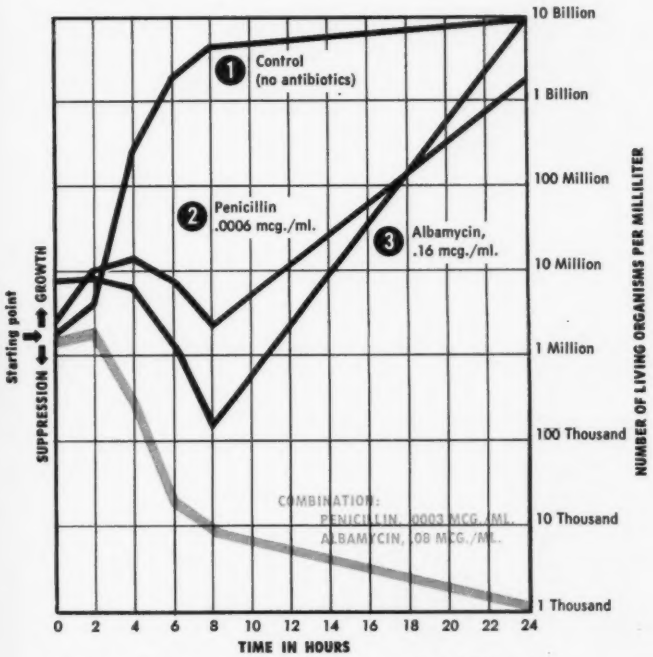

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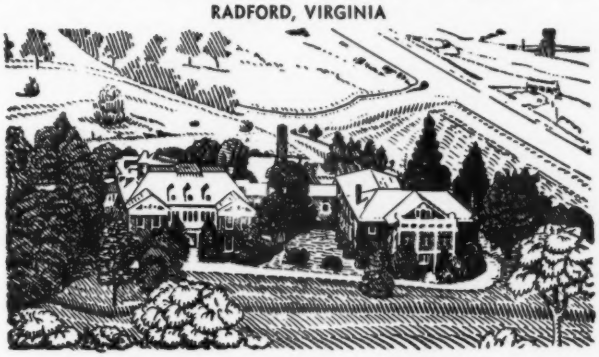

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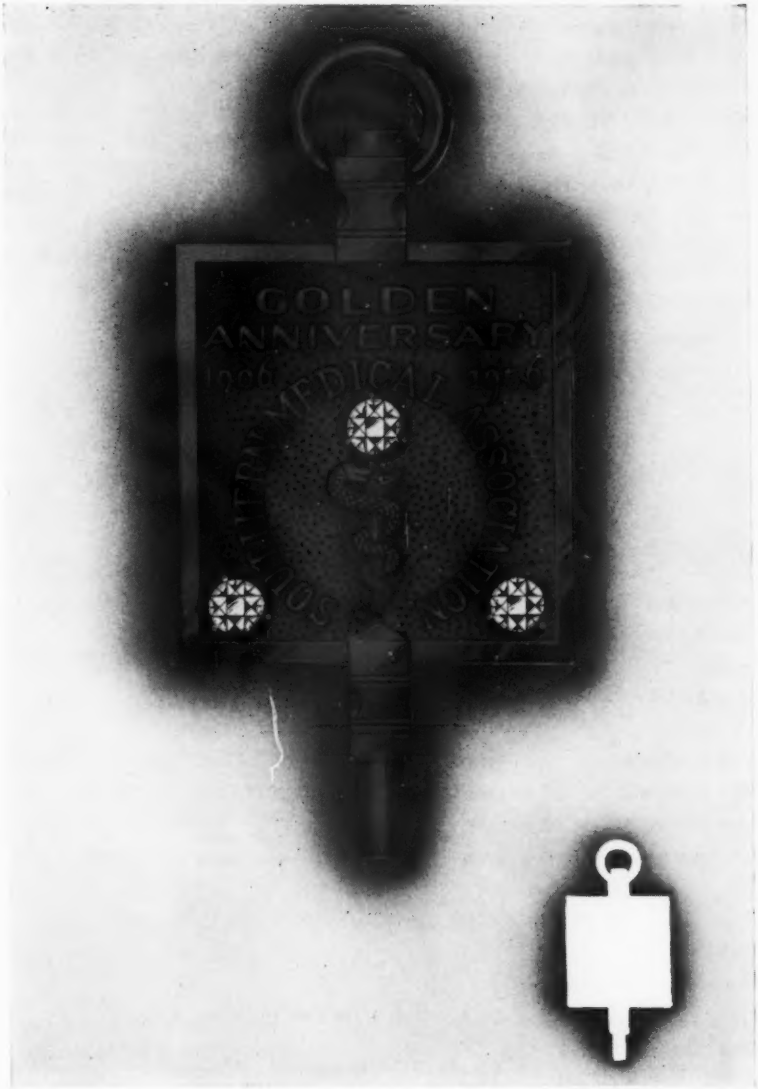

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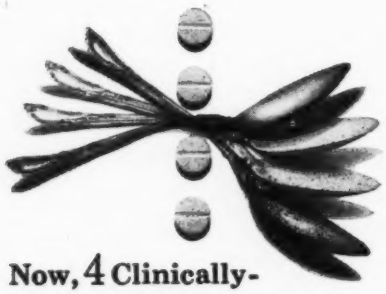

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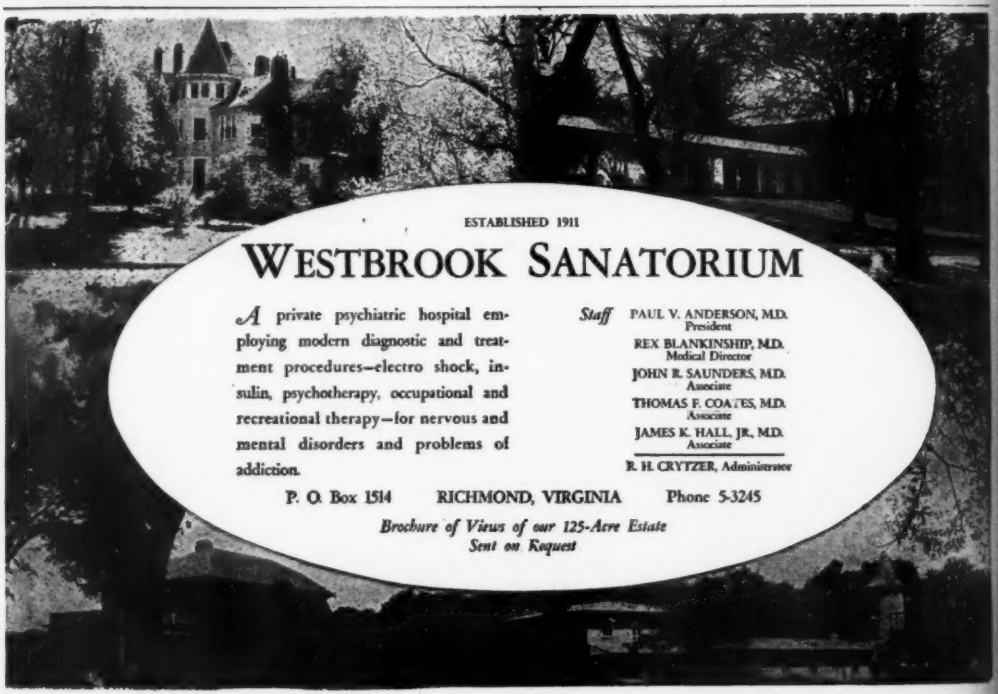

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Penicillin V c̄ Sulfonamides

- Mixed infections
- Undiagnosed infections

PEN•VEE SULFAS is a combination for *wide* antimicrobial action. It offers the advantages of new *acid-stable* penicillin V complemented by the sulfonamides preferred for high effectiveness and increased renal safety. The combined agents permit broadened therapy in numerous infections involving both gram-positive and gram-negative organisms.

Supplied: PEN•VEE SULFAS Tablets, bottles of 36. Each tablet contains 90 mg. (150,000 units) of penicillin V, 0.25 Gm. of sulfadiazine, and 0.25 Gm. of sulfamerazine. Also available: PEN•VEE•*Oral*® Tablets, 300 mg. (500,000 units), bottles of 12; 125 mg. (200,000 units), bottles of 36. PEN•VEE® *Suspension* (Benzathine Penicillin V), 180 mg. (300,000 units) or 90 mg. (150,000 units) per 5-cc. teaspoonful, bottles of 2 fl. oz.

PEN•VEE® SULFAS

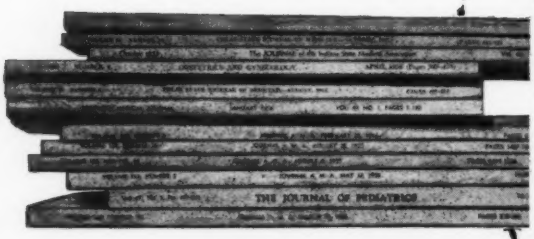
Penicillin V (Phenoxymethyl Penicillin) and Sulfonamides

Wyeth

Philadelphia 1, Pa.

"The average female is borderline iron deficient..."[3]

IN MENSTRUAL



The bibliography specifies

1. Moore, C.V., and Dubach, R.: J.A.M.A. 162:197 (Sept. 15) 1956.
2. Holly, R.G.: Obstet. and Gynec. 2:124 (Aug.) 1953.
3. Ausman, D.C.: Journal-Lancet 76:290 (Oct.) 1956.

LLOYD *Brothers, Inc.*
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ANEMIA...

Evidence shows that practically every menstruating female is in a state of precarious iron balance. Thus the iron deficiency state, due to even *normal* menstrual losses, is an extremely common occurrence.[1, 2]

Correction of this iron deficiency state results in real benefits to the tired, rundown female patient.

Strikingly superior clinical responses in menstrual anemia have been reported with RONCOVITE.[3] These results can be explained by the increased absorption and utilization of iron due to the improved bone marrow activity provided only by RONCOVITE.

Roncovite Tablets (*in menstrual anemia*):

Maximum Adult Dosage: One tablet after each meal and at bedtime.

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THE ORIGINAL, CLINICALLY PROVED COBALT-IRON PRODUCT

for added certainty

in antibiotic therapy...

multi-spectrum†
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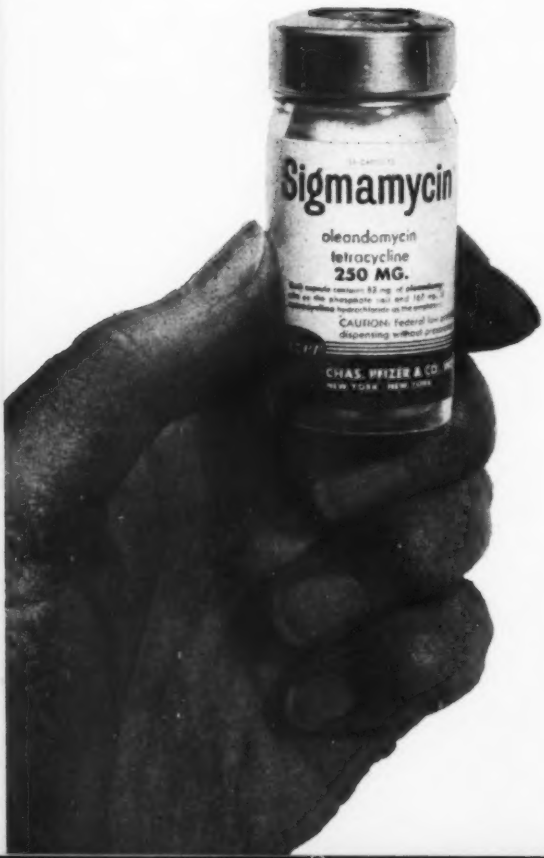

†the antimicrobial spectrum of tetracycline extended and potentiated to include even those strains of staphylococci and other pathogens resistant to previously employed antibiotic therapy; and to provide

1. a new maximum in therapeutic efficacy

2. a new maximum in protection against resistance

3. a new maximum in safety and toleration

Capsules: 250 mg. (oleandomycin 83 mg., tetracycline 167 mg.)

Pfizer *World leader in antibiotic development and pro*

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plus a new maximum in palatability... *now available with new mint-flavored*

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OLEANDOMYCIN TETRACYCLINE

for ORAL SUSPENSION

A savory mint flavor that adds the further certainty of acceptability to antibiotic therapy, particularly for that 90% of the patient population treated in the home or office where sensitivity testing may not be feasible, and where pleasant flavor can make the difference between prescription adherence and laxity.

Sigmamycin for Oral Suspension
is available in 2 oz. bottles containing 1.5 Gm. of Sigmamycin (oleandomycin 500 mg., tetracycline 1 Gm.). When reconstituted each 5 cc. teaspoonful contains 125 mg. of Sigmamycin (42 mg. of oleandomycin as the phosphate salt with tetracycline amphoteric equivalent to 83 mg. of tetracycline hydrochloride).

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a highlight in therapeutics

ACHROMYCIN*

Hydrochloride
Tetracycline HCl Lederle

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acknowledged as competent

Spontaneously acknowledged by physicians everywhere as an outstanding therapeutic advance, repeatedly confirmed during more than three years of clinical usage, ACHROMYCIN Tetracycline ranks among the foremost in its field today . . . judged on its exceptional effectiveness against a wide range of pathogens, prompt control of infections most commonly encountered in medical practice, low incidence of side reactions, minimal emergence of resistance.

ACHROMYCIN is available in 21 dosage forms—each with full tetracycline effect—to meet the exacting requirements of modern medicine.

Lederle LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

Continued from page 141

meritorious sharing in the service of rhinology" at the recent meeting.

The following physicians have been elected to the staff of the Louisiana State University School of Medicine: Drs. Victor Halperin, Alfred Y. K. Hew, and Lawrence L. Swan, assistant professors of pathology; Dr. Murrel H. Kaplan, assistant professor of medicine; Dr. John B. Bobear, instructor in medicine; Drs. John D. Thompson and Robert J. Trace, instructors in obstetrics and gynecology; Drs. Fred B. Berry, George G. Miles, Melvil B. Myers, Jr., and William W. Ogden, II, instructors in surgery; Dr. Jane A. Carver, instructor in medicine and psychiatry and neurology; Drs. William F. Calhoun, Jr., and Max A. Curry, instructors in pediatrics; Drs. Donald F. Gremillion, Saul F. Landry, Jr., John T. Leckert and Earl A. Munyan, instructors in medicine; Dr. Oscar F. Griffin, instructor in pathology; Dr. Leon J. Joseph, instructor in obstetrics and gynecology; Dr. Amzi Denbo Montgomery, instructor in otorhinolaryngology; Dr. Marion A. Guidry, research associate in biochemistry and pathology.

Dr. Malcolm P. Schwarzenbach has been elected president of the Visiting Staff of Charity Hospital.

The Louisiana Academy of General Practice elected the following members to office at a recent meeting: Dr. Esmond A. Fatter, first vice-president; Dr. Rafael C. Sanchez, secretary; Dr. J. Browne Larose, Jr., director, first district; and Dr. Floyd M. Hindelang, director, second district.

MARYLAND

Dr. Harry M. Robinson, Jr., Baltimore, has been appointed a member of the Council of the Southern Medical Association from Maryland for a regular term of five years which began at the close of the Washington meeting in November, the appointment having been made by the President, Dr. J. P. Culpepper, Jr., Hattiesburg, Mississippi. Dr. Robinson succeeds Dr. J. Morris Reese, Baltimore, whose term expired with the close of the Washington meeting and who, having served the Constitutional limit, was not eligible for reappointment.

Dr. N. Norton Springer of the Veterans Administration, Trenton, has been appointed chief of the neuropsychiatric research unit at the VA hospital in Perry Point, effective November 18.

Dr. Nels A. Nelson, has retired as Director of the Bureau of Venereal Diseases of the Baltimore City Health Department. He was succeeded by Dr. Milton Zises, a Commissioned Officer in the U. S. Public Health Service.

MISSOURI

Dr. O. P. J. Falk, St. Louis, has been appointed a member of the Council of the Southern Medical Association from Missouri for a regular term of five years which began at the close of the Washington meeting in November, the appointment having been made by the President, Dr. J. P. Culpepper, Jr., Hat-

Continued on page 68

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Triethanolamine trinitrate biphosphate, LEEMING, 10 mg.

Sustained

***Usual dose:** Just 1 tablet upon arising and one before the evening meal. Bottles of 50 tablets. THOS. LEEMING & CO., INC., 155 East 44th Street, N.Y. 17, N.Y.

relaxes
both mind
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for the average patient in everyday practice

- well suited for prolonged therapy
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- chemically unrelated to chlorpromazine or reserpine
- does not produce significant depression
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Indications: **anxiety and tension states, muscle spasm.**

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Tranquilizer with muscle-relaxant action

DISCOVERED AND INTRODUCED
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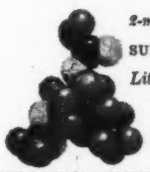
2-methyl-2-n-propyl-1,3-propanediol dicarbamate—U.S. Patent 2,724,720

SUPPLIED: *400 mg. scored tablets. Usual dose: 1 or 2 tablets t.i.d.*

Literature and Samples Available on Request



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When fats upset digestion, it's time to step up the flow of bile

Remington* says: "Bile is essential for the normal digestion of fats and the absorption of fatty acids. The presence of bile in the intestine is also necessary for optimal absorption of the fat-soluble vitmains."

CHOLOGESTIN is a reliable choleretic and cholagogue. It is highly effective because it contains *salicylated bile extract* combined with pancreatin and sodium bicarbonate.

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*Practice of Pharmacy 11th ed., 1956, p. 704.

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you too will
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for monilial vaginitis
it works when others fail

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neomycin and ethamicort
Sig. apply locally b.i.d.
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New Concepts of Optimal Nutrition during THE SECOND FORTY YEARS

Optimal nutrition at all ages is promoted *excellently* by *routine* use of VITA-FOOD Brewers' Yeast: "Brewers' yeast is an excellent source of proteins of high biologic value and of the vitamins of the B complex."[1]

Eminently valuable too are its unsurpassed digestibility, its content of minerals and lipotropic factors, its virtually ideal nutritional *balance*—for normal CO-ACTION of essential nutrients, a synergism indispensable to enduring vigor.[1, 3]

Brewers' yeast is authoritatively attested to be "one of the most useful foods for older people . . . economical . . ."[2] and "frequently helpful in rehabilitating older patients"[3]—in whom the extreme SUBTLETY of cumulative nutritional insults is fostered by TIME, which may also bring increased demands for proteins and vitamins. [1, 3]

For prevention and in dietotherapy of many disorders throughout THE SECOND FORTY YEARS, *prescribe as a routine supplement*

VITA-FOOD Brewers' Yeast

the richest *natural* source of vitamin B complex factors plus nutritionally complete protein, essential minerals and lipotropic factors.

VITAMIN FOOD CO., INC., Newark 4, N. J.

1. McLester and Darby: "Nutrition and Diet in Health and Disease," ed. 6, Saunders, p. 195. 2. McCay, C. M., in Lansing: "Problems of Aging," ed. 3, Williams and Wilkins, 1952, p. 193. 3. Sebrell and Hundley, in Stieglitz: "Geriatric Medicine," ed 3, Lippincott, 1954, p. 189.

Continued from page 64

tiesburg, Mississippi. Dr. Falk succeeds Dr. Grayson Carroll, St. Louis, whose term expired with the close of the Washington meeting and who, having served the Constitutional limit, was not eligible for reappointment.

Dr. Joseph Ogura, St. Louis, has been presented the Golden Head Mirror Award for service in Rhinology by the American Rhinologic Society. Dr. French K. Hansel was elected an honorary member.

Dr. X. J. Masacchia, associate professor at Saint Louis University has been elected to the Corporation of the Marine Biological Laboratory.

Dr. Henry C. Sweany is now director for research, pathology, and allied sciences at the Missouri State Sanatorium in Mount Vernon. Dr. Sweany recently received the medal awarded annually by the American College of Chest Physicians for outstanding contributions in chest pathology.

NORTH CAROLINA

Dr. George D. Wilson, Asheville, is a newly appointed member of the Council of the Southern Med-

Continued on page 72

CLASSIFIED ADVERTISEMENTS

WANTED—EENT Associate, fine southern community, lucrative, long established practice. Contact HP c/o SMJ.

LOCATION WANTED—Internist, 35 years of age, married, board certified; VA training, university affiliated; graduate Minnesota; licensed Minnesota, Missouri; previous group practice experience; completing military service; available January 1957; clinic or group association desired; south or southwest. Reply to ZHN c/o SMJ.

NOTICE—Will the resident in Virginia who contacted box GG in care of the Southern Medical Journal regarding a preceptorship kindly do so again.

ASSOCIATE DESIRED for EENT practice located in large southern medical center. State experience and training. Reply to box GG c/o SMJ.

WANTED—South Central Florida—General Practitioner to take over office of retired doctor; fully equipped 6-room office, including intact patient records; rent $50.00 per month; for details contact: A. L., 67 N. Ridgewood, Sebring, Florida.

RADIUM FOR SALE—Formerly used by Gynecologist. 85 mg. in seven platinum tubes. Contact DM c/o SMJ.

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LOCATION WANTED — General Practitioner, 34 years, would like location in Texas or Oklahoma or would consider other state. Has Texas and Oklahoma license. Can furnish excellent references. Contact AE c/o SMJ.

Romilar
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relieves cough—

...specifically,
by direct suppression
of the cough reflex.
But unlike narcotics,
Romilar does not cause
central depression,
drowsiness, constipation,
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Available as syrup,
tablets, and expectorant
(c NH_4Cl).

Romilar® HBr – brand of dextromethorphan HBr

in a single tablet—

pain relief

plus

antibacterial action

AZO GANTRISIN

In urinary tract infections, Azo Gantrisin usually provides effective antibacterial control (local and systemic), together with prompt relief of associated pain and discomfort . . . by combining well-tolerated Gantrisin with a clinically proved urinary analgesic.

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Each Azo Gantrisin tablet contains 0.5 Gm Gantrisin 'Roche' plus 50 mg phenylazo-diamino-pyridine HCl.

Gantrisin® - brand of sulfisoxazole

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Medication and Adapter fit into neat plastic case, convenient for pocket or purse . . .

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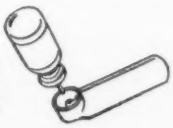
Means an unbreakable Oral Adapter—no movable parts—no glass to break—no rubber to deteriorate . . .



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Means greater economy—no costly glass nebulizers to replace, and one or two inhalations usually suffices for prompt relief.

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The Unique Measured-Dose Inhalation Method

In Asthma

For Rapid Relief of Acute or Continuing Bronchospasm

Medihaler-Epi™

Riker brand of epinephrine 0.5% solution in inert, nontoxic aerosol vehicle. Each ejection delivers 0.125 mg. epinephrine. In 10 cc. vial with metered-dose valve, sufficient for 200 inhalations.

Medihaler-Epi replaces injected epinephrine in emergency situations in which respirations have not ceased. It provides rapid relief in acute food, drug, or pollen reactions (including urticaria, bronchospasm, angioneurotic edema, edema of glottis, etc.). In most instances only one inhalation is necessary.

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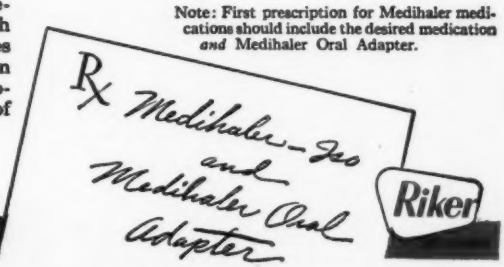
Riker brand of isoproterenol HCl 0.25% solution in inert, nontoxic aerosol vehicle. Each ejection delivers 0.06 mg. isoproterenol. In 10 cc. vial with metered-dose valve, sufficient for 200 inhalations.

Note: First prescription for Medihaler medications should include the desired medication *and* Medihaler Oral Adapter.



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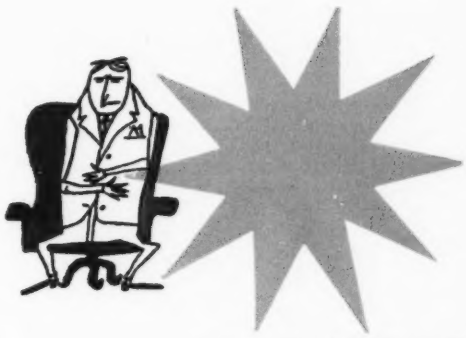

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the most effective anesthetic

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- Quick acting with prolonged effect
- High viscosity and low surface tension permit the anesthetic, Xylocaine Hydrochloride, to come into immediate and intimate contact with the mucous membranes
- Safe . . . nonirritating . . . nonsensitizing.
- Cherry flavored . . . pleasant and easy to take.
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- Contains 2% Xylocaine Hydrochloride in an aqueous solution adjusted to a suitable consistency with carboxymethylcellulose. Cherry flavored for palatability.

Supplied: In bottles of 100 and 450 cc.
Average Dosage: One tablespoonful, administered orally.
Additional information available upon request

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*U.S. Patent No. 2,441,498

Continued from page 68

ical Association from North Carolina for a regular term of five years which began at the close of the Washington meeting in November. The appointment was made by the President, Dr. J. P. Culpepper, Jr., Hattiesburg, Mississippi. Dr. Wilson succeeds Dr. H. L. Brockman, High Point, whose term expired with the close of the Washington meeting and who, having served the Constitutional limit, was not eligible for reappointment. Dr. Wilson has also been elected president-elect of the American Academy of Physical Medicine and Rehabilitation.

Dr. Leslie B. Hohman of Duke University School of Medicine, has been named president-elect of the American Psychopathological Association.

Dr. Isaac M. Taylor, assistant professor of medicine at the University of North Carolina was one of the physicians who treated the survivors of the antarctic plane crash recently near McMurdo Sound. Dr. Taylor is on leave from the University. He left last year for the base, where he will be stationed for approximately 15 months.

Dr. Charles L. Johnston, Jr., recently joined the staff of the Department of Physiology of the University of North Carolina School of Medicine. He is a research associate working with Dr. John Howard Ferguson, professor of physiology.

Dr. Paul M. Gross, vice president and dean of Duke University announced the following new faculty members: Drs. William D. deGravelles, Jr., visiting assistant

Continued on page 76

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your patients are beginning to expect it.....

Just as the "health I.Q." of the general public has increased in recent years, so also has the awareness of diagnostic and therapeutic measures been broadened. The authoritative reassurance of a cardiogram recorded in your own office can be as helpful to your patients as the early diagnosis of heart disease can be to your own clinical management.

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— provides time-saving features and precision engineering for accurate, dependable diagnostic service. Timing and leads are marked automatically, and leads can be switched rapidly without base line shift or distortion. Preset controls simplify operation.

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A specific immunizing antigen for prevention of mumps in children and adults where indicated. Immunizes for about one year.

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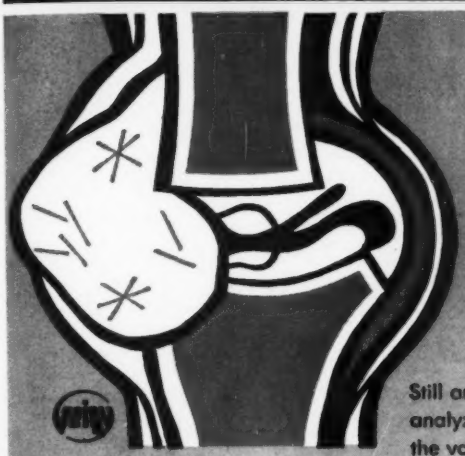
"...clinically useful and effective..."[1]

in relieving arthritis and allied disorders

BUTAZOLIDIN

(phenylbutazone GEIGY)



Still another clinical report, based on a carefully analyzed series of 205 cases, has confirmed the value of BUTAZOLIDIN in arthritis and allied disorders: "Therapeutic effects... are, as a rule, quickly obtained and are easily maintained, and are usually noted within one week."[1]

In short-term therapy, in such conditions as acute gouty arthritis or bursitis, BUTAZOLIDIN generally effects complete relief of pain, and often, equally complete resolution of inflammation, within a period of a few days.

In long-term therapy for the more chronic arthritides, BUTAZOLIDIN in minimal required dosage (sometimes as little as 100 mg. daily) effectively retards the arthritic process with a gratifyingly low incidence of relapse.[2]

BUTAZOLIDIN being a potent therapeutic agent, physicians unfamiliar with its use are urged to send for detailed literature before prescribing it.

1. Denko, C. W., Rumi, D., and Bergenstal, D. M.: Am. Pract. & Digest Treat. 6:1865, 1955.
2. Holbrook, W. P.: M. Clin. North America 39:405, 1955.

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NERVOUS AND MENTAL DISEASES

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A private hospital for diagnosis and treatment of psychiatric and neurological patients. Hospital and out-patient services.

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r coughs associated with the common cold as well as allergic or non-allergic coughs
on-narcotic, but compatible with commonly used narcotic salts
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lower blood pressure WITHOUT JOLTING
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when blood pressure must drift down . . . not plunge
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Dosage: In blood pressures over 200 systolic, 2 tablets four times daily. In other cases, 1 or 2 tablets every four to six hours. Supplied: Bottles of 100 and 1,000
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Continued from page 72

professor of rehabilitation; John M. Rhoads, associate professor of psychiatry; Norman Kirschner, associate in biochemistry; Charles L. Remmel, assistant professor of radiology; John Coughlin, associate in anesthesiology; and Aaron P. Sanders, associate in radiology and director of the Isotope Laboratory.

OKLAHOMA

Drs. S. D. Barnes and J. G. Casey announce the opening of a new doctors' clinic at 117 North Second Street in Hollis.

Drs. Paul C. Gallaher, Shawnee, and J. F. Simons, Alva, were recently presented a Certificate of Appreciation for 10 years service by the Selective Service System.

Dr. C. E. Northcutt, Ponca City, has been added to the board of directors of the Oklahoma Alcoholism Association.

SOUTH CAROLINA

Dr. Vernon B. Moore, Greenwood, has been appointed to the Committee on Maternal Health.

Nine South Carolinians have been accepted as fellows of the American College of Surgeons. They are: Drs. S. Edward Izard, Vernon B. Moore, Homer J. Hancock, George F. West, Norman D. Ellis, Phillips L. Bates, James Allen, Samuel H. Huff, Wendell H. Tiller.

Dr. Malcolm U. Dantzler, Georgetown, has been awarded a United States Public Health Service Traineeship for graduate study in the field of public health administration.

Dr. Benjamin O. Stands, Columbia, has been appointed chairman of the Richland County Red Cross blood program for 1956-57.

Dr. James Arthur Dunlap, Jr., announces the opening of the Ruby Medical Clinic.

Dr. Charles N. Wyatt, Greenville, replaces Dr. Hervey W. Mead, Pendleton, as president of the South Carolina Chapter of the American Academy of General Practice.

TENNESSEE

Drs. Ralph L. Brickell, Jr., and Wilfred L. Wiser, Tullahoma, announce the opening of the Brickell-Wiser Clinic for the practice of medicine and surgery.

New officers of the Memphis Obstetrical and Gynecological Society are: Drs. Carey Bringle, president; William Mackey, vice-president; and Robert Ruch, secretary.

Dr. James M. Tuholski, Memphis, has been named Assistant Director of Clinical Research for Mead Johnson & Co.

Dr. Phineas Jack Sparer, Memphis, has joined the staff of the University of Tennessee College of medicine as professor of psychiatry and preventive medicine.

Dr. Ralph F. Morton, instructor in medicine, University of Tennessee, is the first recipient of the Riley Houck Investigatorship established by the Tennessee Heart Association.

Dr. William A. Nelson has been named first president of the newly formed Knoxville Society of Internal Medicine. Other officers of the group are: Dr. Harold Neuenschwander, vice-president; Dr. Frank London, secretary; and Dr. Kenneth Hicks, treasurer. Drs. Charles Sienknecht and Julian Lentz were elected to the executive council.

Drs. D. C. King and H. W. Thomas, Henderson, have purchased the Steadman-Guy Clinic and it is now known as the Henderson Clinic.

The Southern Trudeau Society recently elected Dr. R. B. Turnbull, Memphis, as vice-president.

Dr. R. M. McCown, Jefferson City, has recently been honored for his 35 years of service to the Carson-Newman football squad.

TEXAS

Dr. Milford O. Rouse, Dallas, first vice-president of the Southern Medical Association, has been chosen an advisory member of the American Medical Education Foundation. This honor is bestowed on persons prominent in medical affairs who have shown an active interest in the foundation.

Dr. John L. Goforth, Dallas, has been elected president of the American Society of Clinical Pathologists.

Dr. Charles J. Wilson, Galveston, has been appointed senior assistant surgeon in the United States Public Health Service Commissioned Reserve.

The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, has appointed Dr. David E. Liston assistant director.

At a recent meeting of the Texas Academy of General Practice the following new officers were elected: Drs. George V. Launey, Dallas, president; G. W. Cleveland, Austin, president-elect; C. E. Oswalt, Fort Stockton, vice-president; and John M. Smith, San Antonio, treasurer.

New officers for the Texas Pediatric Society are: Drs. E. M. Wier, Fort Worth, president; T. J. McElhenney, Austin, president-elect; James N. Walker, Fort Worth, secretary; D. H. McDonald, Abilene, treasurer; and Halcuit Moore, Dallas, councilor for District 2.

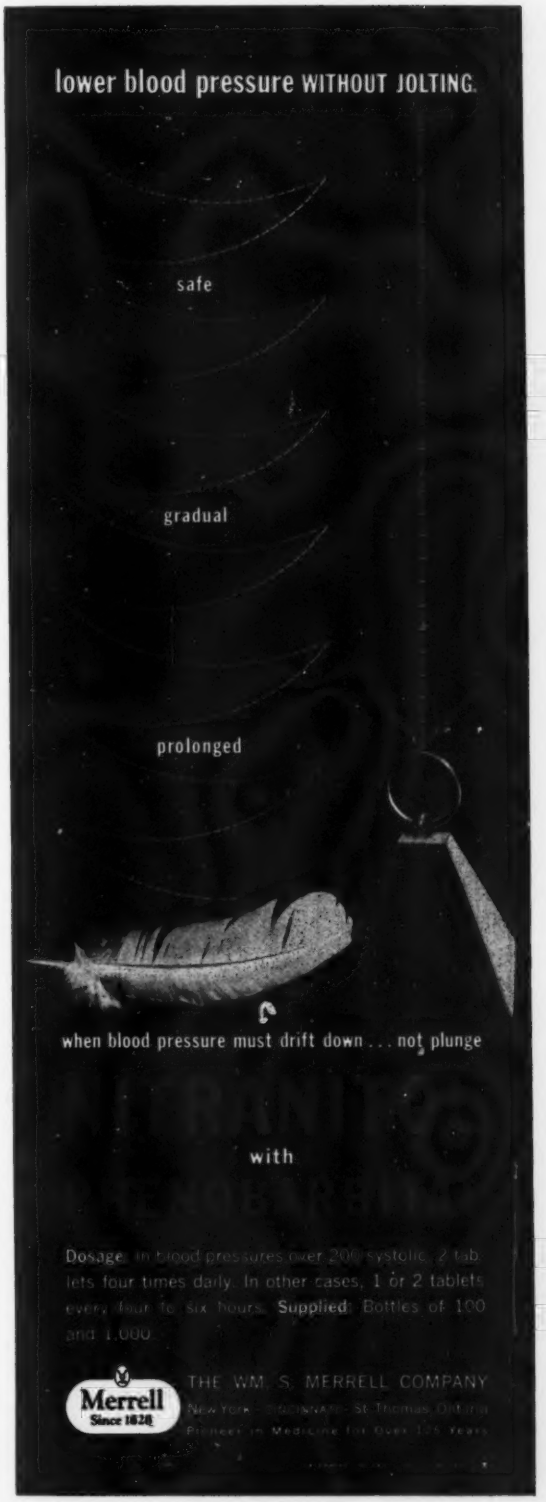
The Temple Division of the University of Texas Postgraduate School of Medicine offers the *Fifth* Scott, Sherwood and Brindley Foundation *Postgraduate Conference* in Medicine and Surgery on March 4, 5, and 6, 1957. For detailed information write: Director, Scott, Sherwood and Brindley Foundation, Scott and White Clinic, Temple, Texas.

VIRGINIA

Dr. H. G. Hudnall, Covington, has been appointed to the medical staff of the Veterans Administration Hospital there.

Dr. Count D. Gibson now serves as acting head of the department of medicine at the Medical College of Virginia. He replaces Dr. Harry Walker. Dr. William F. Maloney has been named Dean of Medicine of the College.

On December 1, Dr. William H. Kelly assumed his duties as assistant director of the Michigan Department of Mental Health.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1. Klemme, H. L.: Clin. Med., October, 1956.

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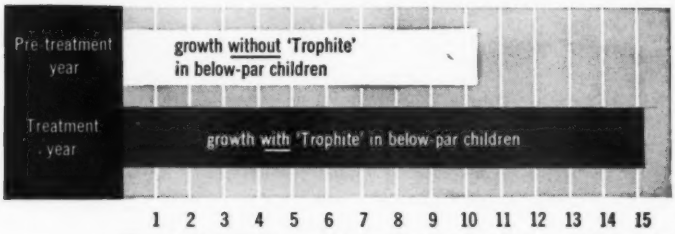
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REFERENCES: 1. Youngblood, V. H.: J. Urol. 70:926, 1953. 2. Powell, E. M., and Wattenberg, C. A.: Tr. Southcentr. Sect. Am. Urol. Ass. Oct. 17-19, 1955. 3. Tudor, J. M.: J. Tennessee M. Ass. 49:181, 1956. 4. MacLeod, P. F.; Rogers, G. S., and Anzlowar, B. R.: Internat. Rec. Med. 169:561, 1956.

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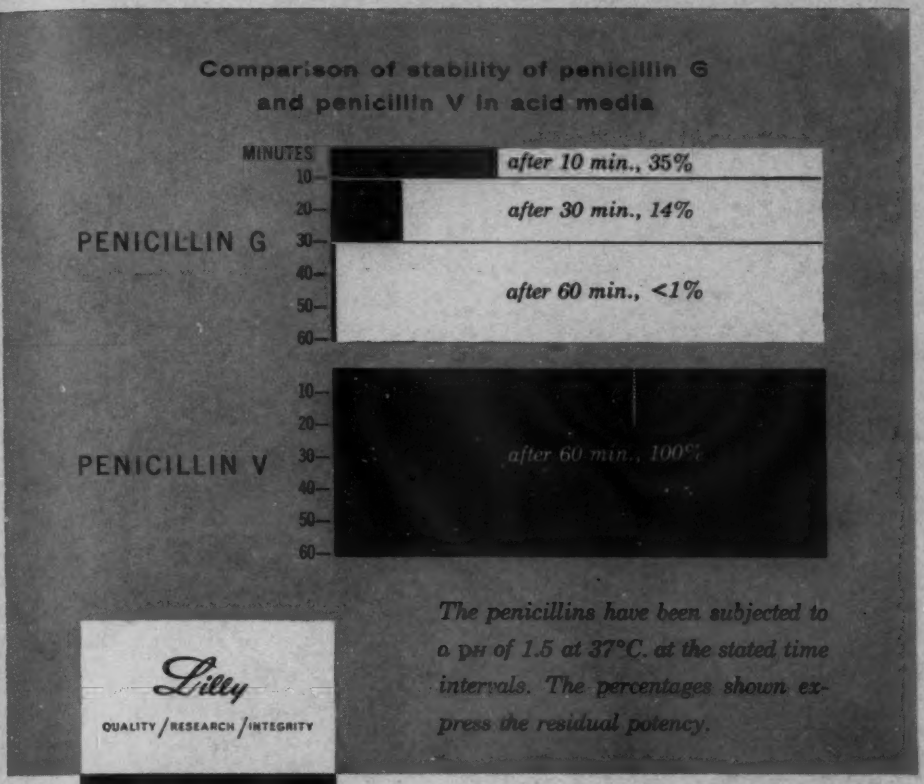
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10
20
30
40
50
60
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after 30 min., 14%
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